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Review article

Getting in touch: A neural model of comforting touch

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ABSTRACT

Comforting touch involves contact distress-alleviating behaviors of an observer towards the suffering of a target. A growing number of studies have investigated the effects of touch on pain attenuation, focusing on the (toucher), the target (comforted) or both. Here we synthesize findings of brain mechanisms underlying comforting touch in the target and toucher to propose an integrative brain model for understanding how touch attenuates distress. Building on evidence from the pain and distress literatures, our model applies interchangeably to pain and distress regulation. We describe comforting touch as a feedback-loop that begins with distress experienced by the target, triggering an empathic response in the toucher which in turn reduces distress in the target. This cycle is mediated by interactions between the neural circuits associated with touch perception, shared distress, emotion regulation and reward as well as brain-to-brain coupling in the observation-execution system. We conclude that formulating a model of comforting touch offers a mechanistic framework for understanding the effects of touch as well as other social interactions involving social support.

1. Comforting touch

The skin is the largest sensory organ covering the whole body, allowing perception and exploration of our surrounding. The sense of touch is believed to be one of the first senses to develop in a human embryo (Gottlieb, 1971). In recent years, it is increasingly acknowledged that beyond the role of touch in perceiving the external world, it is a mediator of several affective and social functions (Cascio et al., 2019). An abundance of adaptive affiliative behaviors including grooming, play and sexual behavior involve touch between individuals, indicating that social touch may have survival advantages (Dunbar and Dunbar, 1998; Panksepp, 1998; Suvilehto et al., 2015). Touch between interacting partners has been shown to affect emotional well-being (Gallace and Spence, 2010) and to regulate stress responses (Grewen et al., 2003), suggesting that certain types of touch serve to relieve distress. While it is known that social mammals demonstrate better recovery from experiences of distress when they are in proximity to a conspecific, a phenomenon termed 'social buffering' (Kikusui et al., 2006), it was suggested that touch is comforting above and beyond mere physical proximity between the target and observer (Nelson and Panksepp, 1998).

Comforting touch may be defined as distress-alleviating contact between an observer and a suffering target. In situations involving suffering, touch may provide physical and emotional relief of distress, beyond what individuals could achieve alone. Comforting touch is not unique to humans. It is a prevalent strategy for distress attenuation across the animal kingdom (Romero et al., 2011), further attesting to its evolutionary role. Consoling behaviors that entail touch were reported in apes (Cordoni et al., 2006; de Waal and van Roosmalen, 1979; Fraser and Aureli, 2008, 2008; Mallavarapu et al., 2006; Romero et al., 2010), large-brained birds (Seed et al., 2007) and dogs (Cools et al., 2008).

A growing body of literature acknowledges the role of social regulation beginning at childhood throughout the life span. These studies highlight the importance of early social interactions in the regulation of the infant's homeostasis, contributing to the basic formation of the self (Fotopoulou and Tsakiris, 2017). Early in their development, humans rely on their social environment to regulate their basic needs (Atzil et al., 2018). The Social Baseline Theory argues that given that self-regulation is metabolically costly, social regulation including comforting touch may diminish the level of effort needed to attenuate distress (Coan and Maresh, 2014). Touch was suggested to play a role in keeping a stable balance among the body's multiple interacting physiological systems during stress (Morrison, 2016). Indeed, various types of comforting touch, including hugging, massage, handholding, or stroking have been

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shown to diminish physical and emotional distress in various social contexts (Coan et al., 2006; Goldstein et al., 2018; Grewen et al., 2003; Kawamichi et al., 2015; Master et al., 2009; von Mohr et al., 2018). Touch was found to attenuate reactivity to stress in infants (Feldman et al., 2010) and the provision of maternal touch in the newborn was shown to enhance social synchrony up until adulthood, contributing to the individual's social skills (Yaniv et al., 2021). Notably, compared to verbal support, comforting touch was found to be more efficient for stress reduction (Ditzen et al., 2007) and the attenuation of social exclusion distress (Morese et al., 2019), demonstrating that it is a powerful strategy for social support.

Despite ample evidence for the beneficial effects of comforting touch, the neural mechanisms that underlie the effects of touch on distress have been examined only in recent years. Neuroimaging studies that have focused on the target of pain demonstrated that social touch is associated with the attenuation of activation in neural networks supporting threat responses (e.g. Coan et al., 2006). On the other hand, studies that focused on the toucher have generally argued that comforting touch represents a basic empathic response of an observer, to the distress of a target (Peled-Avron et al., 2018). While most studies on comforting touch have focused on characterizing either the toucher or the target of distress, emerging studies apply a two-brains approach to examine the effects of touch in interactions consisting of both the target and the toucher.

Here we synthesize disparate findings on touch, empathy and pain, to propose a two-brain model of comforting touch. We argue that comforting touch may be viewed as a feedback loop consisting of a suffering target and an observer/toucher. This feedback loop contains core elements of a regulatory mechanism: an external event, someone else's distress, signals of departure from homeostasis; an empathic response of an observer that triggers touch; regulation of distress through perceiving touch by the target, who returns to homeostasis (Fig. 1). The proposed two-brains neural model explains how various types of touch contribute to distress attenuation. By adopting frameworks from research in the fields of learning and control (Lockwood and Klein-Flügge, 2020) we characterize the way in which feedback from a distressed target can cause the toucher to adapt their touch during comforting touch. The two-brains feedback loop model proposed here may offer a mechanistic framework for understanding the comforting touch as well as other forms of social support, as it allows understanding of both interaction partners as well as providing testable hypotheses regarding the neural underpinnings underlying their behavior.

2. What triggers comforting touch?

Behavioral observations demonstrate that comforting touch occurs when the target experiences physical or emotional pain. For example, studies on consolation in apes show that the initial trigger of consoling touch results from a third party's aggressive acts toward the victim, including physical harm as well as nonphysical acts such as threat (e.g. Romero et al., 2010). Likewise, in humans, it has been shown that comforting touch is used during various types of distress caused by emotional (Cekaite and Kvist Holm, 2017), social (Ditzen et al., 2007) and physical (Coan et al., 2006) insults.

Interestingly, a large body of literature suggests a possible overlap in the neural circuitry underlying physical and social pain (Eisenberger, 2012), indicating that comforting touch may affect the activity of shared neurobiological substrates that underlie both the experiences of physical pain and emotional pain. Neuroimaging studies consistently show that nociceptive stimuli commonly elicit activity in a neural network termed the Pain Matrix (Geha and Waxman, 2016; Ploghaus et al., 1999), a system which involves a very wide array of subcortical and cortical brain structures (Apkarian et al., 2005; Garcia-Larrea et al., 2003), that includes the primary (S1) and secondary (S2) somatosensory cortices, the thalamus, anterior cingulate cortex (ACC) and the insula. Although recent studies have questioned the unitary view of the pain matrix (e.g. Geuter et al., 2020), it is largely agreed that nociceptive stimuli involve a range of networks that could be divided into sensory and affective dimensions, such that the sensory regions (S1 and S2) mediate sensory aspects of pain (e.g. location of pain) while the dorsal ACC (dACC) and

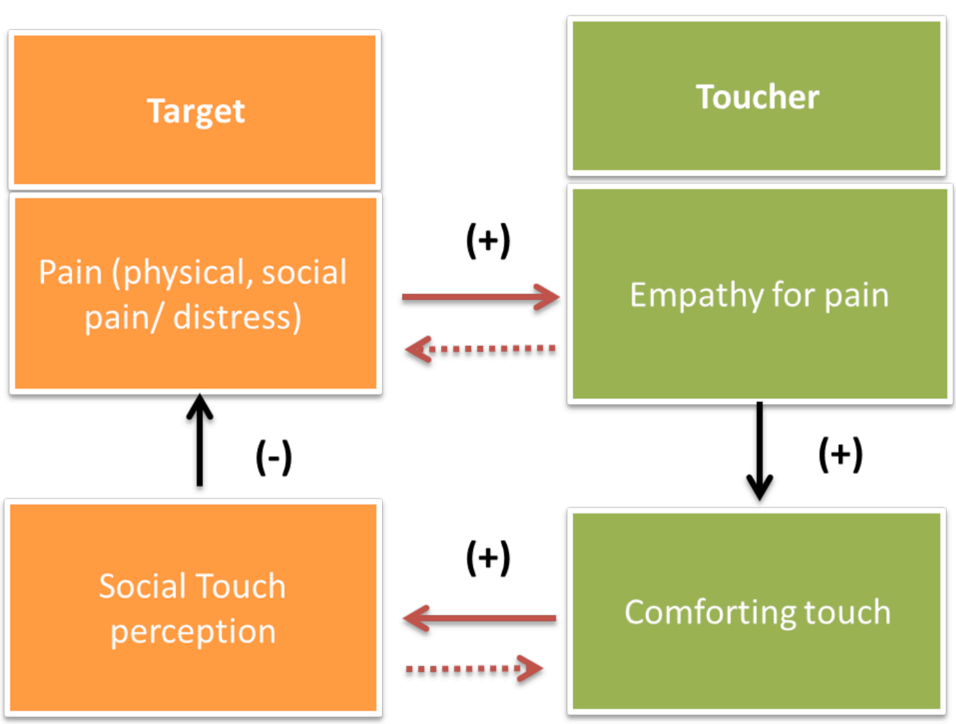

Fig. 1. Comforting touch occurs when the target experiences physical or social pain which triggers empathy for pain in the toucher. The activation of empathy circuits in the toucher may initiate touch which leads to touch perception in the target. Pleasant touch may diminish levels of pain in the target.
(+) represents activation; (-) represents inhibition; solid lines represent unidirectional effects; dashed lines represent possible bidirectional effects.

anterior insula (AI) mediate the affective aspects of pain (Wager et al., 2013). Given the significance of the affective component of pain for signaling unpleasantness and potential harm, it has been hypothesized that social distress (e.g., exclusion) relies on brain regions associated with the affective component of pain (Eisenberger, 2012). Indeed, similar to physical pain, social and emotional pain (e.g. social rejection) has been associated with activity in the dACC (Cacioppo et al., 2013; Eisenberger, 2015; Hsu et al., 2015; Meerwijk et al., 2013; Wager et al., 2009). Notably, beyond shared brain networks there is evidence for dynamic interactions between pain and stress at both the acute and chronic level (Vachon-Presseau, 2018). Furthermore, both stress and pain are jointly modulated by psychosocial factors such as fears, beliefs, goals, and the social context (Karos et al., 2018).

Since comforting touch aims at diminishing distress, it is not surprising that it was found to directly regulate physical and social distress as well as decrease activity in regions related to affective aspects of pain such as the dACC and AI. For example, Coan et al. (2006) found that handholding attenuates activation in the neural systems supporting threat responses. Similarly, in a recent study, López-Solà et al. (2019) found that handholding reduced pain as well as activity in the AI and dACC. These studies indicate that comforting touch may be triggered by pain or pain-related distress occurring to the target. Touch appears to directly affect the activity of core brain regions that contribute to pain and pain-related-affective distress.

3. Comforting touch as an expression of empathy

From the point of view of the toucher, providing comforting touch is a prosocial response driven by empathy, directed towards another person (Romero et al., 2010). Empathy refers to the cognitive and the emotional reactions of an observer towards the distress of the target (Decety and Jackson, 2004; Shamay-Tsoory, 2011). Accumulative evidence suggests that empathy plays an important role in contributing to distress regulation (Decety and Fotopoulou, 2015).

The question remains, how does empathy contribute to attenuating pain? Detecting distress in others does not necessarily lead to action. Empathic responses can be covert and consist of internal emotional changes or inner thoughts that are not communicated back to the target. However, empathic responses are often overt and include detectable facial or body expression, verbal responses or touch. These overt reactions may be communicated back to the target and directly affect her/his emotional state. Given that touching is also rewarding for the toucher (Gentsch et al., 2015), it is not surprising that touch is frequently selected as an empathic response. In line with this, Romero et al. (2010) have suggested that consoling touch in chimpanzees represents an empathic response. Indeed, different variables known to affect empathy, such as social closeness and kinship, affect comforting touch in primates (Fraser and Aureli, 2008). It has been suggested that empathy has a key role in social touch in human as well (Bufalari and Ionta, 2013). Goldstein et al. (2016) found that during handholding, the toucher's level of trait empathy (as measured by the interpersonal reactivity index [IRI]) predicted the level of pain experienced by the target, indicating that highly empathic touchers are better at comforting their partners. This suggests that the effectiveness of touch is moderated by the levels of empathy experienced by the target and that individual differences in the touchers' empathy contribute to the level of pain attenuation.

One possible explanation for these findings is that highly empathic individuals are better at adapting their responses to the target, based on the feedback they receive from the target. It was recently suggested that *adaptive empathy*, a term that denotes the capacity to adapt one's empathic responses to the target, is a central aspect of empathic skills (Hertz and Shamay-Tsoory, 2021). By synthesizing models of empathy with models of learning, the adaptive empathy approach frames empathy as a process that involves a feedback loop, where the likelihood of providing a specific empathic reaction changes during and across interactions, based on feedback from the target (Main et al., 2017; Tamir and Thornton, 2018; Zaki et al., 2008). In line with the adaptive empathy framework, participants with high empathic traits (scoring high on a cognitive empathy scale) were reported to be better at learning about the preferred emotion regulation strategies of different suffering targets, as compared to low empathic participants (Kozakevich-Arbel et al., 2021). Given that emotions are identifiable via touch (Hertenstein et al., 2006), it is likely that highly empathic touchers are capable of identifying the levels of pain communicated by the target and adapt their touch accordingly.

Sharing the pain of a target activates the affective component of the pain network, including the dACC and the AI. On the other hand, the need to align in movement, emotion or cognition during empathy triggers activity in a neural network responsible for observation-execution (mirror) network, including the inferior frontal gyrus (IFG) and inferior parietal lobule (IPL) (Lamm et al., 2011). The activation of this parietofrontal circuit indicates that action representations that are primarily involved in experiencing distress are also recruited during the observation of distress (Rizzolatti and Sinigaglia, 2016). The participation of the shared pain and observation-execution networks in empathy for pain implies that in addition to sharing the distress of the target, empathy entails a matching system that synchronizes the response of the observer to that of the target. In line with this, Korisky et al. (2020) scanned couples during comforting touch and found shared activations between the target and toucher in the IPL. Interestingly, there was a correlation between the IPL activity of the toucher and the target during handholding, pointing to possible coupled activity in the IPL between partners. Likewise, comforting a loved one experiencing pain resulted in changes of physiological rhythms - EEG mu/alpha band (8–12 Hz) suppression - associated with observation-execution: (Peled-Avron et al., 2018). Moreover, in a dual-EEG study, it was found that handholding of romantic couples during pain administration increased brain-to-brain coupling in the alpha-mu band in a network that mainly involves the central regions of the pain in the target, and the right hemisphere of the pain observer (Goldstein et al., 2018). Importantly, the extent of brain-to-brain coupling was found to correlate with the toucher's state empathy. In line with this, in a recent physiological study, Reddan et al. (2020) reported that trait empathy predicted levels of synchrony in skin conductance response in couples during handholding.

Taken together, these studies indicate that comforting touch represents an empathic response of an observer towards the suffering of a target. By means of coupling in the observation-execution systems of the target and the toucher, the toucher may take advantage of their own representations of distress to understand the targets' physical or emotional distress and provide a touch that is attuned to the targets' needs.

4. Types of comforting touch

Touch information is conveyed from the skin to the brain via afferent fibers that innervate distinct classes of mechanoreceptors. It was suggested that the functional division in the neural organization of touch may resemble that of pain, possessing the dissociable sensory and affective dimensions (e.g. Auvray et al., 2010; McGlone et al., 2007). Neuroimaging studies show that affective touch activates the classical somatosensory areas S1 and S2 as well as affective regions, including the posterior contralateral insular cortex and the dACC (e.g. Gordon et al., 2013). Notably, Scalabrini et al. (2019) have shown that touch of animate compared to an inanimate protagonist is perceived as more synchronous with the self and that the spontaneous brain activity in the pregenual ACC (pgACC) can predict the response to animate touch, indicating that the brain is wired to become aligned with touching agents. Indeed, a burgeoning literature has demonstrated that merely observing others' touch involves regions related to direct experienced touch (e.g Gazzola et al., 2012; Sharma et al., 2018).

Still, the activation of touch-related networks largely depends on the type of touch provided. It is well established that large myelinated afferents (Aβ-fibers) convey tactile sensation from both glabrous and hairy skin and are activated by all types of mechanical events, reflecting their importance in discriminative touch (Kandel et al., 2013). Activating Aβ-fibers projects information to the spinal cord and then to the thalamus, which conveys touch signaling to the somatosensory cortex and other multimodal regions. Aβ afferents have fast conductance velocity allowing rapid detection of spatial and temporal tactile information (Vallbo and Johansson, 1984). On the other hand, C-Tactile (CT) afferents in the hairy skin are considered as slow afferents that convey the affective aspects of touch (Olausson et al., 2010). Gentle stroking stimulates the unmyelinated CT afferents that convey tactile sensation (Löken et al., 2009). Neuroimaging findings reveal that CT fibers project to the posterior insular cortex (PI) and the orbitofrontal cortex (OFC) (Björnsdotter and Olausson, 2011; Mcglone et al., 2012). The stimulation of CT afferents was suggested to trigger the release of oxytocin (Walker et al., 2017). Notably, it was recently reported that touch signaling may rely on a population of parvocellular oxytocin neurons in the rat PVN, selective for of affiliative touch (Tang et al., 2020).

Both gentle stroking on hairy skin and handholding were previously associated with comforting responses (Table 1). Considering that the CT afferent system is widely believed to be specialized for affective touch (McGlone et al., 2007), it was proposed to serve as a key mechanism for pain regulation. CT touch was found to be already developed in infancy (Fairhurst et al., 2014), to affect the activity of the autonomic nervous system in infants (Bytomski et al., 2020; Croy et al., 2016; Manzotti et al., 2019; Van Puyvelde et al., 2019), and to attenuate noxious-evoked brain activity in infants (Gursul et al., 2018). von Mohr et al. (2018), found that slow stroking reduced the amplitude of early and late ERPs as well as subjective pain. Likewise, Liljencrantz et al. (2017), reported that slow brushing – optimal for CT activation – is effective in reducing pain from cutaneous heating. Slow stroking was also found to decrease heart rate in adults (Triscoli et al., 2017) and to diminish emotional distress such as feelings of exclusion (von Mohr et al. (2018). Furthermore, individuals with social difficulties (e.g. individuals diagnosed with autism spectrum condition) show attenuation in brain response to CT touch (Kaiser et al., 2016; Silva and Schalock, 2016), further attesting to the social and affective role of this type of touch.

Nonetheless, touch induced-analgesia has also been reported in the context of handholding in several studies (e.g. Goldstein et al., 2016, 2018; Reddan et al., 2020; Che et al., 2018). Graff et al. (2019) reported that participants assigned to a handholding condition compared to the control group showed accelerated habituation to stress and decreased pupil reactivity. Handholding was also found to be effective in reducing distress related to various medical procedures including surgery (Moon and Cho (2001), cystoscopy (Kwon et al. (2018) and cancer treatments (Weekes et al., 1993). It was suggested that the stimulation of Aβ afferents by touching the palm is also pleasurable (Krämer et al., 2007; Mcglone et al., 2012) and similarly activates insular and OFC regions (Rolls et al., 2003). In addition to the OFC and insula, the pgACC has also been found to respond to pleasant touch both in palm touch (Rolls et al., 2003) and during human touch massage (Lindgren et al., 2012). López-Solà et al. (2019) found that handholding reduced pain, attenuated the activity of pain related regions and increased connectivity between the pain networks and both somatosensory and “default mode” regions. In line with this, Kreuder et al. (2018) found that handholding was most effective in reducing the unpleasantness of electric shocks, and intranasal administration of the oxytocin was associated with stronger decrease of neural responses to shocks in the AI and stronger activity in prefrontal regions.

However, the ability of handholding to reduce pain may also depend on the situation in which the pain is experienced. For instance, in a study examining how handholding affected the experience of emotional pain while one member of a romantic couple shared a past emotionally painful experience (Sahi et al., 2021), results showed that handholding increased feelings of comfort in the individual reliving the past emotionally painful experience, but did not specifically reduce emotional pain levels. Instead, the pain-reducing effects of handholding emerged later on. Painful memories recounted while handholding were (weeks to months) later reported to be less painful than painful memories recounted without handholding. Thus, while handholding had a delayed effect on reducing emotional pain, it did not have an immediate effect. One possible explanation for this is that there are some situations in which experiencing pain may be more adaptive. Thus, while fully experiencing an experimental physical pain stimulus is likely not

Table 1
Comparison between handholding and gentle stroking.

	Type of skin	Receptor	Fiber group	Conduction velocity (ms-1, appr. mean values)	Comforting effect
Handholding	glabrous	Low threshold mechanoreceptors-codes all aspects of mechanostimulation	Aβ	60 High temporal and spatial resolution	**Physical pain** Coan et al. (2006) Goldstein et al. (2018) Goldstein et al. (2016) Reddan et al. (2020) López-Solà et al. (2019) Kreuder et al. (2018) Che et al. (2018) **Emotional distress** Graff et al. (2019) Moon and Cho (2001) Kwon et al. (2018) Weekes et al. (1993) Sahi et al. (2021)
Slow stroking	Hairy	Low-threshold mechanoreceptors (CT) Codes specific forces and velocities	C	<2 Poor temporal and spatial resolution	**Physical pain** Gursul et al. (2018) Liljencrantz et al. (2017) von Mohr et al. (2018), Reddan et al. (2020) **Emotional distress** Van Puyvelde et al. (2019) von Mohr et al. (2018), Van Puyvelde et al. (2019) von Mohr et al. (2018)

helpful, it might be useful to fully experience a past emotionally painful experience in order to process it more fully and learn from it. Hence, there may be some situations in which certain kinds of emotionally painful experiences are not immediately reduced by handholding.

As shown in Table 1, there is strong evidence supporting the effectiveness of both handholding and slow stroking in pain and distress reduction. While both types of touch are effective strategies for comfort, it is possible that there are individual differences in touch preference. Krahé et al. (2016) have shown that the effects of touch interact with the attachment style of the participant, such that the effects of touch depend on the expectations of the target from social support. Moreover, individual differences in narcissism have also been shown to mediate the correlation between spontaneous and task-induced activity in AI during touch (Scalabrini et al., 2017). Given that the effects of touch largely depend on culture and types of relationships (Sorokowska et al., 2021), it may be suggested that both external and internal context may mediate the effect of touch.

5. Closing the loop: when pain and touch interact

The evidence reported above indicates that the neural mechanisms underlying the effects of touch on distress may be related to several mechanisms by which touch-related neural activity interacts with pain/distress networks. Given that pain is multidimensional and includes physical, emotional and interpersonal aspects (Hadjistavropoulos et al., 2004), the question remains which aspect of pain signaling interacts with touch. Early studies have proposed that touch-induced analgesia, attributed to A-beta activation, is mediated by the gating of nociceptive input at the spinal level whereby touch closes the spinal nerve "gates" to painful input, preventing pain signaling traveling to the brain (Melzack, 1996). Yet it is increasingly acknowledged that touch-pain interactions also take place at cortical-subcortical networks (Mancini et al., 2015), suggesting that the analgesic effects attributed to touch are based on the inhibitory effect that somatosensory fibers (A-beta and CT) have on pain fibers, in addition to the impact of affective processes. Given that touch also affects emotional and social distress, it is possible that mechanisms underlying the effects of touch on distress may be related to several mechanisms by which touch-related neural activity interacts with the affective dimension of pain.

The prominent findings of coupling of autonomic (Goldstein et al., 2018; Reddan et al., 2020) and brain (Goldstein et al., 2018; Korisky et al., 2020) activity between the toucher and the target indicate that bidirectional information flow between interaction partners is essential for pain attenuation. Coupled brain activity between the target and the toucher during comforting touch was mainly found in regions related to the observation-execution system. As described above, Korisky et al. (2020) reported similar activity in the IPL between the target and the toucher during handholding. Notably, evidence from hyper-scanning fNIRS studies points to brain-to-brain coupling in observation-execution related regions such as the inferior frontal gyrus (IFG) and IPL during various types of social interactions (Nguyen et al., 2020; Osaka et al., 2015; Nguyen et al., 2020). Specifically, the IPL was reported to be coupled between participants during social interactions that involve cooperation (e.g. Miller et al., 2019) and joint action (Chen et al., 2020). Furthermore, coupling between IPL of interaction partners was found to predict better connectedness between them, including working alliance in psychotherapy (Zhang et al., 2018) and increased affiliation between strangers (Kinreich et al., 2017). Importantly, coupling in the observation-execution system was found to be a core component of social alignment (Shamay-Tsoory et al., 2019).

Considering that during comforting touch, brain-to-brain coupling in the observation-execution system increases, it is possible that touch may serve as a channel for the generation of alignment between the toucher and target at multiple levels. Alignment in emotion, cognition and motion may allow better information transfer between partners and thus reduce distress. In line with this, synchronized body motion during psychotherapy was demonstrated to predict better outcome of treatment (Ramseyer and Tschacher, 2011). In the case of touch, the information transferred between partners may include level of distress (target) or empathy (toucher). Notably, Hertenstein et al. (2006) found that information regarding emotions is transferred via touch. Specifically, it was reported that participants were able identify various emotions including love and sympathy from the experience of being touched on the arm (without seeing the toucher). This indicates that touch can reliably communicate emotions and that the receiver is able to recognize the emotion communicated by the toucher (Hertenstein, 2002; Hertenstein et al., 2006). If indeed touch increases social alignment, it is possible that both the toucher and the target are able to share their emotions during touch.

Moreover, the mutual alignment that develops during handholding may also signal to the target that the toucher understands their distress and may consequently help them. Feeling understood is known to alleviate negative affect (Seehausen et al., 2012). Morelli et al. (2014) have reported that understanding feelings may activate parts of the reward circuitry including the ventral striatum (VS). In line with this, Reddan et al. (2020) have recently reported that higher levels of activation in the striatum predicted lower levels of pain during handholding. Lindgren et al. (2012) reported that pleasurable touch massage most strongly activates part of the reward circuitry including the pgACC. Interestingly, it has been shown that parts of the reward system (e.g. OFC) are not only active during first-hand experience of touch but also during vicarious touch (Lamm et al., 2015). Likewise, findings on resting-state connectivity shows shared activity in the ventromedial prefrontal cortex (VMPFC) during self and other representation (Murray et al., 2015), indicating that both the target and the toucher share the rewarding experience of touch. It is thus possible that this shared experience helps the target to feel understood and this may interact with the pain representation in a way that alleviates the threat associated with the painful stimulus.

Yet, the question remains: how does reward attenuate distress? One possibility is that reward may affect pain through mutually inhibitory effects of pain and pleasure processing. Pleasure-related analgesia is reported in various situations including sexual behaviour (Forsberg et al., 1987), viewing pictures of loved ones (Master et al., 2009) and pleasurable music (Roy et al., 2008). Ecological studies on facial expression show that people experiencing intense negative or positive affect—for example, pain or orgasm—spontaneously produce facial expressions that are undistinguishable (Aviezer et al., 2012). Notably, it has been suggested that pleasure and pain share similar mechanisms, pointing to potentially reciprocal inhibitory mechanisms which may take place in brain areas in which adjacent subregions encode aversive and appetitive processing (Leknes and Tracey, 2008). For example, it has been suggested that different OFC subregions represent pleasant touch and pain (Rolls et al., 2003). Similarly, it has been reported that the pgACC is activated by positive rewards while dACC responds to punishment (Liu et al., 2011). Indeed, Vogt (2005), suggested that while both the pgACC and dACC mediate pain, the pgACC is more related to pleasure, indicating that pain attenuation might be resolved in the context of the cingulate subregions. Accordingly, functional interactions between pain and pleasure subregions within the ACC and the OFC may serve as a potential mechanism by which touch mitigates pain. Notably it was reported that CT touch activates parts of the reward circuitry including the striatum and OFC (Sailer et al., 2016). In line with this, it was demonstrated that optimal C-touch (slow, gentle touch on the forearm) is more likely than other types of touch to convey arousal, lust or desire (Kirsch et al., 2018), indicating that stroking may attenuate pain by enhancing pleasure.

The reward account of comforting touch is also supported by findings showing that people's feelings towards the person that touches them plays an important role in mediating the effects of touch (Coan et al., 2006; Goldstein et al., 2016). Several brain regions, including S1 and the ACC (Gazzola et al., 2012) and the OFC (McCabe et al., 2008) were found to react differently, depending on the protagonist that touches the subject. This suggests that the attitudes and feelings towards the toucher may increase activity in the pleasant touch network. In fact, it was reported that the mere representation of a loved one may attenuate pain ratings as compared to experiencing the pain alone (Master et al., 2009). Furthermore, it was suggested that touch serves as a safety signal and that even touch provided by a machine or an animal is comforting (Eckstein et al., 2020), indicating that beyond the fiber stimulated, stimuli associated with touch may be comforting.

These findings are in line with studies demonstrating that reward circuitry plays a key role in placebo analgesia (Scott et al., 2008). It is thus possible that comforting touch diminishes levels of distress by modifying one's expectations about pain. This view is consistent with studies showing that touch provided by a romantic partner increases the availability of μ-opioid receptors in reward-related neural regions (Nummenmaa et al., 2016).

Yet another possibility is that the rewarding effects of touch may interfere with pain processing by distracting the target's attention from the pain. Distraction is an emotion regulation strategy that involves deploying attention away from the emotionally salient aspects of an emotion-eliciting event (Urry, 2010). Emotion regulation refers to how individuals attempt to influence the way they experience emotions (Gross, 2008). According to the distraction explanation, distress is reduced during touch because the target's attention shifts from the distress stimuli to the rewarding touch stimuli. The dACC-AI involvement in both social pain and physical pain may underlie this effect. The overlap in dACC-AI activity in both pain and pleasure may represent the role of this system in signaling salient events (Iannetti et al., 2013). In line with this, Dalgleish et al. (2017) showed that the dACC and AI are commonly activated by feedback from negative and positive cues. Thus, activation of this network in the context of touch may compete with the activation of this system generated by pain, thus attenuating pain.

Beyond brain-to-brain coupling and reward, it is possible that other mechanisms related to emotion regulation are activated during comforting touch. As mentioned earlier, Korisky et al. (2020) found coupled activation in the IPL between the target and the toucher. Psychophysiological interaction (PPI) analysis was carried out to examine brain regions in which activity was coupled with the IPL in the target. This analysis revealed that the IPL activity during handholding was positively coupled with activity in the dorsomedial prefrontal cortex, a region that has been implicated in emotion regulation. Similar findings were reported by López-Solà et al. (2019) who found that handholding increased functional connectivity between the pain related regions and the medial prefrontal cortices. This may indicate that increased functional integration between pain and emotion regulation processing may take place during comforting touch. Previous studies have highlighted the importance of the prefrontal cortex in emotion regulation and in the ability to downregulate negative emotions (see Etkin et al., 2015; Ochsner and Barrett, 2001). It is possible that external support encourages reappraisal of pain intensity and may influence levels of pain experienced by the target. Indeed, it was argued that social support during pain fosters reassessment of the threat stimuli and may thus attenuate pain (Krahé et al., 2013). This suggests that comforting touch may contribute to the target's ability to self-regulate their distress by increasing prefrontal activity. While this view seemingly contradicts the Social Baseline Theory, according to which touch may allow diminished regulatory efforts of the target (Coan and Sbarra, 2013), differences in the timing of touch may explain the incongruity between these explanations. It is possible that touch has an initial rapid effect reducing prefrontal activity which is followed by a prolonged stage involving higher efficacy of self-regulation. It may be speculated that in the initial phase of comforting touch, when expecting pain, there is decrease in frontal activity while during pain itself there is increase in frontal activity.

Finally, although the proposed neural model focuses on the reward, distress and observation-execution systems, other networks may be involved in this cycle. The mentalizing system and regions that mediate self-other distinction (e.g. temporo-pariental junction) may also be involved in comforting touch, as it involves self-other overlap as well as understanding the intentions of others. Furthermore, given that the toucher also experiences touch and vicarious pleasant touch (Morrison et al., 2011) these regions are probably also activated in the toucher.

6. Characterizing the comforting touch feedback loop

The evidence presented above demonstrates that comforting touch involves a dynamic interaction between the target and the toucher whereby the toucher attempts to attenuate the distress of the target by adapting the touch to the target's needs. Several core brain networks comprise the comforting touch feedback-loop (Fig. 2), which occurs in six phases:

1) As in regulatory mechanisms, the loop commences as an external event, someone's distress, which signals the departure from homeostasis. This external event activates the pain/distress network in the target.
2) The toucher identifies the target's affective state, and shares this state. Distress sharing involves activation of the distress network (dACC, AI) as well as the observation-execution system responsible for adjusting responses to the target over time.
3) The toucher initiates social touch activating touch networks.
4) The target identifies the touch provided and aligns with the target's touch. Note that the observation-execution network facilitates *mutual* alignment between the target and the toucher and is coupled between individuals.
5) As the target identifies that her/his distress was reliably communicated to the toucher, top-down processes are activated, including the reward/valuation system which signals connectedness, and the emotion regulation network responsible for regulating pain and social distress.
6) The toucher is able to gain tactile information on the target, which can help increase mutual alignment and adaptive empathy. The reward system, which has been shown to participate in support provision (Inagaki and Eisenberger, 2012) is also activated, signaling that the comforting touch obtained the expected support.

The cycle may continue as the toucher detects changes in the levels of distress in the target. The adaptive empathy approach, discussed above, argues that the reward/valuation system, which reacts to changes in the environment, mostly those associated with positive outcomes, tracks changes in the target's distress based on feedback (Hertz and Shamay-Tsoory, 2021). Based on this framework, the reward system may assign value to the toucher's reactions and therefore contribute to adapting the responses based on feedback from the target. This idea is compatible with principles of reinforcement learning and predictive coding according to which regulatory mechanisms track trial-by-trial learning from feedback (Huang and Rao, 2011; Rescorla and Wagner, 1972; Sutton and Barto, 2012; Wolpert et al., 1995).

The predictive coding approach assumes that individuals continually change their behaviors based on predictions about the outcome of their behaviors (Daw et al., 2005). According to this theory, the brain essentially generates predictions based on previous information (top-down signals) in order to predict the outcomes of different responses. When the incoming information (bottom-up signal) is different from the prediction (outcome of a response), that constitutes a prediction error. The brain can then either amend the response, or alternatively update the prediction based on the bottom-up information (Spratling, 2017). In this framework, touch can be considered as a response that is aimed at reducing the target's distress while the target's homeostasis is the predicted outcome of touch related actions (Fig. 3). When the type/intensity of touch applied has fallen short of the expected reduced distress, there is a negative prediction error. These distress-regulation

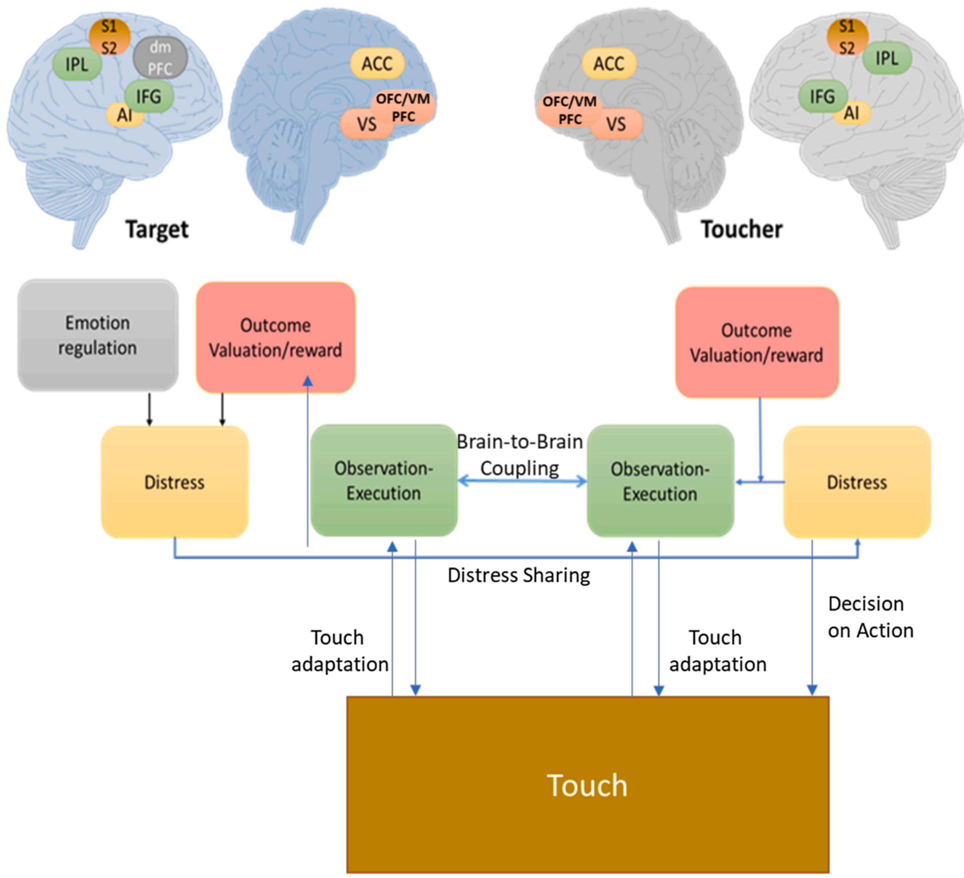

Fig. 2. Proposed feedback-loop model of comforting touch. When the target experiences physical or emotional pain a 'shared pain' network (yellow) is activated in the target and then in the toucher. The activity of the observation-execution systems (green) between partners is coupled during touch, allowing mutual alignment. The mechanisms of pain attenuation in the target involves the interactions between pleasant touch network (reward-VS, OFC, VMPFC) and pain network (AI, ACC) including interactions within sub-regions and coupling between these systems and reward mechanisms (red). In addition, interactions between emotion regulation networks (gray) and pain network may also contribute to pain relief in the consoled. The valuation and reward system in the target, including the ventral striatum, may identify the outcome of the selected touch, and send signals to adapt future responses. Abbreviations: IPL-inferior parietal lobule; IFG- inferior frontal gyrus; S1- primary somatosensory cortex; S2-secondary somatosensory cortex; dmPFC-dorsomedial prefrontal cortex; OFC-orbitofrontal cortex; VMPFC-ventromedial prefrontal cortex; VS-ventral striatum; AI-anterior insula; ACC-anterior cingulate cortex.

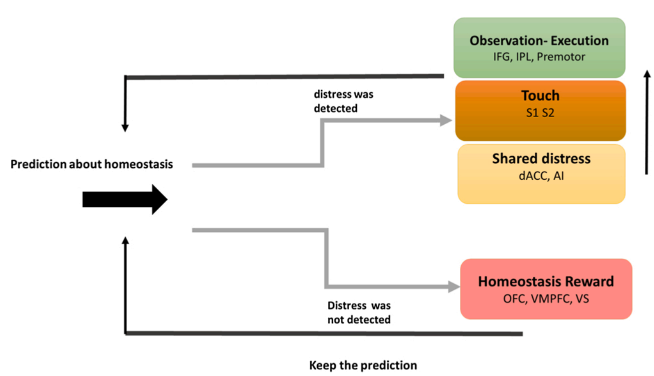

Fig. 3. The Predictive Model of Comforting Touch. According to the predictive coding framework of comforting touch the brain constantly generates predictions of the expected homeostasis. A prediction error occurs when the incoming information about the other's distress is different from the prediction. Detecting a distress activates the shared distress, touch and observation execution systems whereas detecting homeostasis activates the reward system. Abbreviations: IPL-inferior parietal lobule; IFG- inferior frontal gyrus; S1- primary somatosensory cortex; S2- secondary somatosensory cortex; OFC-orbitofrontal cortex; VMPFC-ventromedial prefrontal cortex; VS-ventral striatum; AI-anterior insula; dACC-dorsal anterior cingulate cortex.

prediction errors update the value of a specific touch. The type or intensity of touch applied is based on its predicted outcome, i.e., on the expected ability to relieve the target's distress. The outcome of each response is compared with its expected outcome, and any mismatch between expectation and outcome serves as a prediction error used to adapt future responses. For example, when a high pressure/intensity of touch is ineffective, the toucher updates the prediction and decreases the pressure. Such updates may take place based on associative learning where the association between touch response and its distress relief is learned during a specific interaction or across interactions (Fig. 3).

This proposed 'loop' is homeostatic as it includes a corrective mechanism. This indicates that during comforting touch achieving homeostasis in the target serves as the optimization principle, as it reduces prediction errors, lowering the computational cost of social processing (also referred to as "minimizing free energy" (Koban et al., 2017)).

The same principles of prediction coding may also be applied to the target. This view is in line with the 'Mentalizing Homeostasis' approach (Fotopoulou and Tsakiris, 2017) according to which predictive processes are at the heart of social regulation. This framework proposes that touch plays a key role in homeostatic regulation of the target (Fotopoulou and Tsakiris, 2017; von Mohr and Fotopoulou, 2018).

The feedback loop model may explain a range of findings related to comforting touch. For example, the model may explain the added value of touch over other factors related to pain attenuation including mere presence or perceived empathy of the toucher. While previous studies have suggested that perceived levels of empathy of an observer may affect the pain of a target (Hurter et al., 2014; Sambo et al., 2010), the model predicts that the extent to which the toucher adapts the touch based on feedback is critical for pain attenuation, beyond perceived empathy.

Relatedly, the comforting touch feedback loop model may also explain the previously described negative effects of empathy and solicitous support in both experimental and clinical settings. Solicitous support represents conditions in which the target of pain is provided with extra care resulting in negative pain outcomes (Boothby et al., 2004). Here we hold that adaptation of the responses based on feedback is a core component of comforting touch and responding in a manner that in not attuned with the target's needs (too much care or too little care) may have detrimental outcomes.

Finally, given that different types of touch activate different pathways, it is possible that handholding and stroking mediate pain reduction by different mechanisms.

While the CT system may mediate passively received touch from other people and overlaps with neurobiological systems of reward signaling, handholding is more 'equal' and involves reciprocal communication of touch and allows both partners to communicate their emotions.

7. Conclusions

Although it is common knowledge that touch attenuates distress, only in recent years have we begun to understand the neural mechanisms underlying this behavior. Much research has examined the target and the toucher separately, as they are both constructs of significant relevance to understanding comforting touch. Here we synthesize different lines of studies into an integrative model of comforting touch, examining the contribution of empathy to distress attenuation during touch. Building on studies from both the pain and distress literatures, we offer a model of comforting touch that explains pain and distress regulation. We put forward a two-brains approach that broadens our understanding of social touch to include both the target and the toucher in one feedback loop. The feedback loop starts with a distress experienced by a target, continues with an empathic response of the toucher, which is followed by reward signaling and emotion regulation in the target. Building on the predictive coding framework, we suggest that comforting touch involves a dynamic interaction between the target and the toucher whereby the toucher attempts to attenuate the distress of the target by adapting the touch to the target's needs. The outcome of each response is compared with its expected outcome, and gaps between expectation and outcome serve as a prediction error used to adapt touch characteristics. Though the aforementioned findings support each of the steps outlined in this feedback loop model, more research is needed to confirm the cyclical nature of these steps and how the neural mechanisms of both the target and the toucher interact in a reciprocal manner. We believe that beyond comforting touch, characterizing this feedback loop model may provide a valuable opportunity for understanding various types of interactions that involve social support.

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References

Apkarian, A.V., Bushnell, M.C., Treede, R.D., Zubieta, J.K., 2005. Human brain mechanisms of pain perception and regulation in health and disease. Eur. J. Pain 9 (4), 463. https://doi.org/10.1016/j.ejpain.2004.11.001.

Atzil, S., Gao, W., Fradkin, I., Barrett, L.F., 2018. Growing a social brain. Nat. Hum. Behav. 2 (9), 624–636. https://doi.org/10.1038/s41562-018-0384-6.

Auvray, M., Myin, E., Spence, C., 2010. The sensory-discriminative and affective-motivational aspects of pain. Neurosci. Biobehav. Rev. 34 (2), 214–223. https://doi.org/10.1016/j.neubiorev.2008.07.008. Pergamon.

Aviezer, H., Trope, Y., Todorov, A., 2012. Body cues, not facial expressions, discriminate between intense positive and negative emotions. Science 338 (6111), 1225–1229. https://doi.org/10.1126/science.1224313.

Björnsdotter, M., Olausson, H., 2011. Vicarious responses to social touch in posterior insular cortex are tuned to pleasant caressing speeds. J. Neurosci. 31 (26), 9554–9562. https://doi.org/10.1523/JNEUROSCI.0397-11.2011.

Boothby, J.L., Thorn, B.E., Overduin, L.Y., Ward, L.C., 2004. Catastrophizing and perceived partner responses to pain. Pain 109 (3), 500–506. https://doi.org/10.1016/J.PAIN.2004.02.030.

Bufalari, I., Ionta, S., 2013. The social and personality neuroscience of empathy for pain and touch. Front. Hum. Neurosci. 7 (July), 393. https://doi.org/10.3389/fnhum.2013.00393.

Bytomski, A., Ritschel, G., Bierling, A., Bendas, J., Weidner, K., Croy, I., 2020. Maternal stroking is a fine-tuned mechanism relating to C-tactile afferent activation: an exploratory study. Psychol. Neurosci. 13 (2), 149–157. https://doi.org/10.1037/PNE0000184.

Cacioppo, S., Frum, C., Asp, E., Weiss, R.M., Lewis, J.W., Cacioppo, J.T., 2013. A quantitative meta-analysis of functional imaging studies of social rejection. Sci. Rep. 3 (1), 1–3. https://doi.org/10.1038/srep02027.

Cascio, C.J., Moore, D., McGlone, F., 2019. Social touch and human development. Dev. Cogn. Neurosci. 35, 5–11. https://doi.org/10.1016/j.dcn.2018.04.009.

Cekaite, A., Kvist Holm, M., 2017. The comforting touch: tactile intimacy and talk in managing children's distress. Res. Lang. Soc. Interact. 50 (2), 109–127. https://doi.org/10.1080/08351813.2017.1301293.

Che, X., Cash, R., Fitzgerald, P., Fitzgibbon, B.M., 2018. The social regulation of pain: autonomic and neurophysiological changes associated with perceived threat. J. Pain 19 (5), 496–505. https://doi.org/10.1016/J.JPAIN.2017.12.007.

Chen, Y., Zhang, Q., Yuan, S., Zhao, B., Zhang, P., Bai, X., 2020. The influence of prior intention on joint action: an fNIRS-based hyperscanning study. Soc. Cogn. Affect. Neurosci. 2020, 1–10. https://doi.org/10.1093/scan/nsaa152.

Coan, J.A., Maresh, E.L., 2014. Social baseline theory and the social regulation of emotion. Handbook of Emotion Regulation, pp. 221–236. https://psycnet-apa-org.ezproxy.haifa.ac.il/record/2013-44085-014.

Coan, J.A., Sbarra, D.A., 2013. Psychophysiology of relationships. Int. J. Psychophysiol. 88 (3).

Coan, J.A., Schaefer, H.S., Davidson, R.J., 2006. Lending a hand: social regulation of the neural response to threat. Psychol. Sci. 17 (12), 1032–1039. https://doi.org/10.1111/j.1467-9280.2006.01832.x.

Cools, A.K.A., Van Hout, A.J.M., Nelissen, M.H.J., 2008. Canine reconciliation and third-party-initiated postconflict affiliation: Do peacemaking social mechanisms in dogs rival those of higher primates? Ethology 114 (1), 53–63. https://doi.org/10.1111/j.1439-0310.2007.01443.x.

Cordoni, G., Palagi, E., Tarli, S.B., 2006. Reconciliation and consolation in captive western gorillas. Int. J. Primatol. 27 (5), 1365–1382. https://doi.org/10.1007/s10764-006-9078-4.

Croy, I., Luong, A., Triscoli, C., Hofmann, E., Olausson, H., Sailer, U., 2016. Interpersonal stroking touch is targeted to C tactile afferent activation. Behav. Brain Res. SreeTestContent1 297, 37–40. https://doi.org/10.1016/J.BBR.2015.09.038.

Dalgleish, T., Walsh, N.D., Mobbs, D., Schweizer, S., Van Harmelen, A.L., Dunn, B., Dunn, V., Goodyer, I., Stretton, J., 2017. Social pain and social gain in the adolescent brain: a common neural circuitry underlying both positive and negative social evaluation. Sci. Rep. 7 (1), 1–8. https://doi.org/10.1038/srep42010.

Daw, N.D., Niv, Y., Dayan, P., 2005. Uncertainty-based competition between prefrontal and dorsolateral striatal systems for behavioral control. Nat. Neurosci. 8 (12), 1704–1711. https://doi.org/10.1038/nn1560.

de Waal, F.B.M., van Roosmalen, A., 1979. Reconciliation and consolation among chimpanzees. Behav. Ecol. Sociobiol. 5 (1), 55–66. https://doi.org/10.1007/BF00302695.

Decety, J., Fotopoulou, A., 2015. Why empathy has a beneficial impact on others in medicine: unifying theories. Front. Behav. Neurosci. (January), 457. https://doi.org/10.3389/FNBEH.2014.00457.

Decety, J., Jackson, P.L., 2004. The functional architecture of human empathy. Behav. Cogn. Neurosci. Rev. 3 (2) https://doi.org/10.1177/1534582304267187.

Ditzen, B., Neumann, I.D., Bodenmann, G., von Dawans, B., Turner, R.A., Ehlert, U., Heinrichs, M., 2007. Effects of different kinds of couple interaction on cortisol and heart rate responses to stress in women. Psychoneuroendocrinology. https://doi.org/10.1016/j.psyneuen.2007.03.011.

Dunbar, R., Dunbar, R.I.M., 1998. Grooming, Gossip, and the Evolution of Language - Robin Dunbar, Robin Ian MacDonald Dunbar - Google Books. Harvard University Press. https://books.google.co.il/books?hl=en&lr=&id=nN5DFNT-6ToC&oi=fnd&pg=PA1&dq=Dunbar,+R.+and+R.+I.+M.+Dunbar+(1998).+Grooming,+gossip+and+the+evolution+of+language,+Harvard+University+Press.&ots=71D73-aMWd&sig=YzoOC-Nxu2LAYtyH80T_bc_-R6Y&redir_esc=y#v=onepa.

Eckstein, M., Mamaev, I., Ditzen, B., Sailer, U., 2020. Calming effects of touch in human, animal, and robotic interaction—scientific state-of-the-Art and technical advances. Front. Psychiatry 11, 555058. https://doi.org/10.3389/FPSYT.2020.555058.

Eisenberger, N.I., 2012. The pain of social disconnection: examining the shared neural underpinnings of physical and social pain. Nat. Rev. Neurosci. 13 (6), 421–434. https://doi.org/10.1038/nrn3231. Nature Publishing Group.

Eisenberger, N.I., 2015. Social pain and the brain: controversies, questions, and where to go from Here. Annu. Rev. Psychol. 66 (1), 601–629. https://doi.org/10.1146/annurev-psych-010213-115146.

Etkin, A., Büchel, C., Gross, J.J., 2015. The neural bases of emotion regulation. Nat. Rev. Neurosci. 16 (11), 693–700. https://doi.org/10.1038/nrn4044.

Fairhurst, M.T., Löken, L., Grossmann, T., 2014. Physiological and Behavioral Responses Reveal 9-Month-Old Infants' Sensitivity to Pleasant Touch. Psychol. Sci. 25 (5), 1124–1131. https://doi.org/10.1177/0956797614527114.

Feldman, R., Singer, M., Zagoory, O., 2010. Touch attenuates infants' physiological reactivity to stress. Dev. Sci. 13 (2), 271–278. https://doi.org/10.1111/J.1467-7687.2009.00890.X.

Forsberg, G., Wiesenfeld-Hallin, Z., Eneroth, P., Södersten, P., 1987. Sexual behavior induces naloxone-reversible hypoalgesia in male rats. Neurosci. Lett. 81 (1–2), 151–154. https://doi.org/10.1016/0304-3940(87)90356-9.

Fotopoulou, A., Tsakiris, M., 2017. Mentalizing homeostasis: the social origins of interoceptive inference. Neuropsychoanalysis 19 (1), 3–28. https://doi.org/10.1080/15294145.2017.1294031.

Fraser, O.N., Aureli, F., 2008. Reconciliation, consolation and postconflict behavioral specificity in chimpanzees. Am. J. Primatol. 70 (12), 1114–1123. https://doi.org/10.1002/ajp.20608.

Gallace, A., Spence, C., 2010. The science of interpersonal touch: an overview. Neurosci. Biobehav. Rev. 34 (2), 246–259. https://doi.org/10.1016/j.neubiorev.2008.10.004. Pergamon.

Garcia-Larrea, L., Frot, M., Valeriani, M., 2003. Brain generators of laser-evoked potentials: from dipoles to functional significance. Neurophysiol. Clin. Neurophysiol. 33 (6), 279–292. https://doi.org/10.1016/j.neucli.2003.10.008.

Gazzola, V., Spezio, M.L., Etzel, J.A., Castelli, F., Adolphs, R., Keysers, C., 2012. Primary somatosensory cortex discriminates affective significance in social touch. Proc. Natl. Acad. Sci. U. S. A. 109 (25), 9688. https://doi.org/10.1073/pnas.1113211109.

Geha, P., Waxman, S.G., 2016. Pain perception: multiple matrices or one? JAMA Neurol. 73 (6), 628–630. https://doi.org/10.1001/jamaneurol.2016.0757. American Medical Association.

Gentsch, A., Panagiotopoulou, E., Fotopoulou, A., 2015. Active interpersonal touch gives rise to the social softness illusion. Curr. Biol. 25 (18), 2392–2397. https://doi.org/10.1016/J.CUB.2015.07.049.

Geuter, S., Reynolds Losin, E.A., Roy, M., Atlas, L.Y., Schmidt, L., Krishnan, A., Koban, L., Wager, T.D., Lindquist, M.A., 2020. Multiple brain networks mediating stimulus–Pain relationships in humans. Cereb. Cortex 30 (7), 4204–4219. https://doi.org/10.1093/CERCOR/BHAA048.

Goldstein, P., Shamay-Tsoory, S.G., Yellinek, S., Weissman-Fogel, I., 2016. Empathy predicts an experimental pain reduction during touch. J. Pain 17 (10), 1049–1057. https://doi.org/10.1016/j.jpain.2016.06.007.

Goldstein, P., Weissman-Fogel, I., Dumas, G., Shamay-Tsoory, S.G., 2018. Brain-to-brain coupling during handholding is associated with pain reduction. Proc. Natl. Acad. Sci. U. S. A. 115 (11), E2528–E2537. https://doi.org/10.1073/pnas.1703643115.

Gordon, I., Voos, A.C., Bennett, R.H., Bolling, D.Z., Pelphrey, K.A., Kaiser, M.D., 2013. Brain mechanisms for processing affective touch. Hum. Brain Mapp. 34 (4), 914–922. https://doi.org/10.1002/hbm.21480.

Gottlieb, G., 1971. Ontogenesis of sensory function in birds and mammals. The Biopsychology of Development, pp. 67–128.

Graff, T.C., Luke, S.G., Birmingham, W.C., 2019. Supportive hand-holding attenuates pupillary responses to stress in adult couples. PLoS One 14 (2), e0212703. https://doi.org/10.1371/JOURNAL.PONE.0212703.

Grewen, K.M., Anderson, B.J., Girdler, S.S., Light, K.C., 2003. Warm partner contact is related to lower cardiovascular reactivity. Behav. Med. 29 (3), 123–130. https://doi.org/10.1080/08964280309596065.

Gross, J.J., 2008. Emotion regulation. Handbook of Emotions 3 (3), 497–513.

Gursul, D., Goksan, S., Hartley, C., Mellado, G.S., Moultrie, F., Hoskin, A., Adams, E., Hathway, G., Walker, S., McGlone, F., Slater, R., 2018. Stroking modulates noxious-evoked brain activity in human infants. Curr. Biol. 28 (24), R1380–R1381. https://doi.org/10.1016/J.CUB.2018.11.014.

Hadjistavropoulos, H.D., Asmundson, G.J.G., Kowalyk, K.M., 2004. Measures of anxiety: is there a difference in their ability to predict functioning at three-month follow-up among pain patients? Eur. J. Pain 8 (1), 1–11. https://doi.org/10.1016/S1090-3801(03)00059-4.

Hertenstein, M.J., 2002. Touch: its communicative functions in infancy. In: Human Development, Vol. 45. www.karger.comwww.karger.com/journals/hde.

Hertenstein, M.J., Keltner, D., App, B., Bulleit, B.A., Jaskolka, A.R., 2006. Touch communicates distinct emotions. Emotion 6 (3), 528–533. https://doi.org/10.1037/1528-3542.6.3.528.

Hertz, U., Shamay-Tsoory, S., 2021. Adaptive Empathy: a Model for Learning Empathic Responses Based on Feedback. https://doi.org/10.31234/OSF.IO/JUC87.

Hsu, D.T., Sanford, B.J., Meyers, K.K., Love, T.M., Hazlett, K.E., Walker, S.J., Mickey, B. J., Koeppe, R.A., Langenecker, S.A., Zubieta, J.K., 2015. It still hurts: altered endogenous opioid activity in the brain during social rejection and acceptance in major depressive disorder. Mol. Psychiatry 20 (2), 193–200. https://doi.org/10.1038/mp.2014.185.

Huang, Y., Rao, R.P.N.N., 2011. Predictive coding. Wiley Interdiscip. Rev. Cogn. Sci. 2 (5), 580–593. https://doi.org/10.1002/wcs.142.

Hurter, S., Paloyelis, Y., Amanda, A.C., Fotopoulou, A., 2014. Partners' empathy increases pain ratings: effects of perceived empathy and attachment style on pain report and display. J. Pain 15 (9), 934–944. https://doi.org/10.1016/j.jpain.2014.06.004.

Iannetti, G.D., Salomons, T.V., Moayedi, M., Mouraux, A., Davis, K.D., 2013. Beyond metaphor: contrasting mechanisms of social and physical pain. Trends Cogn. Sci. 17 (8), 371–378. https://doi.org/10.1016/j.tics.2013.06.002. Elsevier Current Trends.

Inagaki, T.K., Eisenberger, N.I., 2012. Neural correlates of giving support to a loved one. Psychosom. Med. 74 (1), 3–7. https://doi.org/10.1097/PSY.0b013e3182359335.

Kaiser, M.D., Yang, D.Y.-J., Voos, A.C., Bennett, R.H., Gordon, I., Pretzsch, C., Beam, D., Keifer, C., Eilbott, J., McGlone, F., Pelphrey, K.A., 2016. Brain mechanisms for processing affective (and nonaffective) touch are atypical in autism. Cereb. Cortex 26 (6), 2705–2714. https://doi.org/10.1093/CERCOR/BHV125.

Kandel, E.R., Schwartz, J.H., Jessell, T.M., Siegelbaum, S.A., Hudspeth, A.J.H., 2013. Principles of Neural Science.

Karos, K., Williams, A.C.C., Meulders, A., Vlaeyen, J.W.S., 2018. Pain as a threat to the social self: a motivational account. Pain 159 (9), 1690–1695.

Kawamichi, H., Kitada, R., Yoshihara, K., Takahashi, H.K., Sadato, N., 2015. Interpersonal touch suppresses visual processing of aversive stimuli. Front. Hum. Neurosci. 9 (April), 1–11. https://doi.org/10.3389/fnhum.2015.00164.

Kikusui, T., Winslow, J.T., Mori, Y., 2006. Social buffering: relief from stress and anxiety. Philos. Trans. R. Soc. B: Biol. Sci. 361 (1476), 2215–2228. https://doi.org/10.1098/RSTB.2006.1941.

Kinreich, S., Djalovski, A., Kraus, L., Louzoun, Y., Feldman, R., 2017. Brain-to-Brain synchrony during naturalistic social interactions. Sci. Rep. 7 (1), 1–12. https://doi.org/10.1038/s41598-017-17339-5.

Kirsch, L.P., Krahé, C., Blom, N., Crucianelli, L., Moro, V., Jenkinson, P.M., Fotopoulou, A., 2018. Reading the mind in the touch: neurophysiological specificity in the communication of emotions by touch. Neuropsychologia 116, 136–149. https://doi.org/10.1016/J.NEUROPSYCHOLOGIA.2017.05.024.

Koban, L., Ramamoorthy, A., Konvalinka, I., 2017. Why do we fall into sync with others? Interpersonal synchronization and the brain's optimization principle. Soc. Neurosci. 14 (1), 1–9. https://doi.org/10.1080/17470919.2017.1400463.

Korisky, Adi, Eisenberger, N.I., Nevat, M., Weissman-Fogel, I., Shamay-Tsoory, S.G., 2020. A dual-brain approach for understanding the neuralmechanisms that underlie the comforting effects of social touch. Cortex 127, 333–346. https://doi.org/10.1016/j.cortex.2020.01.028.

Kozakevich-Arbel, E., Shamay-Tsoory, S., Hertz, U., 2021. Adaptive Empathy: empathic response selection as a dynamic, feedback-based learning process. Front. Psychiatry 12, 1248.

Krahé, C., Springer, A., Weinman, J.A., Fotopoulou, A., 2013. The social modulation of pain: others as predictive signals of salience – a systematic review. Front. Hum. Neurosci. https://doi.org/10.3389/fnhum.2013.00386.

Krahé, C., Drabek, M.M., Paloyelis, Y., Fotopoulou, A., 2016. Affective touch and attachment style modulate pain: a laser-evoked potentials study. Philos. Trans. Biol. Sci. 371 (1708) https://doi.org/10.1098/RSTB.2016.0009.

Krämer, H.H., Lundblad, L., Birklein, F., Linde, M., Karlsson, T., Elam, M., Olausson, H., 2007. Activation of the cortical pain network by soft tactile stimulation after injection of sumatriptan. Pain 133 (1–3), 72–78. https://doi.org/10.1016/j.pain.2007.03.001.

Kreuder, A.K., Wassermann, L., Wollseifer, M., Ditzen, B., Eckstein, M., Stoffel-Wagner, B., Hennig, J., Hurlemann, R., Scheele, D., 2018. Oxytocin enhances the pain-relieving effects of social support in romantic couples. Hum. Brain Mapp. 40 (1), 242–251. https://doi.org/10.1002/HBM.24368.

Kwon, W.-A., Lee, J.W., Seo, H.K., Oh, T.H., Park, S.C., Jeong, H.J., Seo, I.Y., 2018. Hand-holding during cystoscopy decreases patient anxiety, pain, and dissatisfaction: a pilot randomized controlled trial. Urol. Int. 100 (2), 222–227. https://doi.org/10.1159/000485745.

Lamm, C., Decety, J., Singer, T., 2011. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. NeuroImage 54 (3), 2492–2502. https://doi.org/10.1016/j.neuroimage.2010.10.014.

Lamm, C., Silani, G., Singer, T., 2015. Distinct neural networks underlying empathy for pleasant and unpleasant touch. Cortex 70, 79–89. https://doi.org/10.1016/J.CORTEX.2015.01.021.

Leknes, S., Tracey, I., 2008. A common neurobiology for pain and pleasure. Nat. Rev. Neurosci. 9 (4), 314–320. https://doi.org/10.1038/nrn2333. Nature Publishing Group.

Liljencrantz, J., Strigo, I., Ellingsen, D.M., Krämer, H.H., Lundblad, L.C., Nagi, S.S., Leknes, S., Olausson, H., 2017. Slow brushing reduces heat pain in humans. Eur. J. Pain (UK) 21 (7), 1173–1185. https://doi.org/10.1002/ejp.1018.

Lindgren, L., Westling, G., Brulin, C., Lehtipalo, S., Andersson, M., Nyberg, L., 2012. Pleasant human touch is represented in pregenual anterior cingulate cortex. NeuroImage 59 (4), 3427–3432. https://doi.org/10.1016/j.neuroimage.2011.11.013.

Liu, X., Hairston, J., Schrier, M., Fan, J., 2011. Common and distinct networks underlying reward valence and processing stages: a meta-analysis of functional neuroimaging studies. Neurosci. Biobehav. Rev. 35 (5), 1219–1236. https://doi.org/10.1016/j.neubiorev.2010.12.012. Pergamon.

Lockwood, P.L., Klein-Flügge, M.C., 2020. Computational modelling of social cognition and behaviour—a reinforcement learning primer. Soc. Cogn. Affect. Neurosci. 2019 (August), 1–11. https://doi.org/10.1093/scan/nsaa040.

Löken, L.S., Wessberg, J., Morrison, I., Mcglone, F., Olausson, H., 2009. Coding of Pleasant Touch by Unmyelinated Afferents in Humans. https://doi.org/10.1038/nn.2312.

López-Solà, M., Geuter, S., Koban, L., Coan, J.A., Wager, T.D., 2019. Brain mechanisms of social touch-induced analgesia in females. Pain 160 (9), 2072–2085. https://doi.org/10.1097/j.pain.0000000000001599.

Main, A., Walle, E.A., Kho, C., Halpern, J., 2017. The interpersonal functions of empathy: a relational perspective. Emot. Rev. 9 (4), 358–366. https://doi.org/10.1177/1754073916669440.

Mallavarapu, S., Stoinski, T.S., Bloomsmith, M.A., Maple, T.L., 2006. Postconflict behavior in captive western lowland gorillas (Gorilla gorilla gorilla). Am. J. Primatol. 68 (8), 789–801. https://doi.org/10.1002/ajp.20279.

Mancini, F., Beaumont, A.-L., Hu, L., Haggard, P., Iannetti, G.D.D., 2015. Touch inhibits subcortical and cortical nociceptive responses. Pain 156 (10), 1936. https://doi.org/10.1097/J.PAIN.0000000000000253.

Manzotti, A., Cerritelli, F., Esteves, J.E., Lista, G., Lombardi, E., La Rocca, S., Gallace, A., McGlone, F.P., Walker, S.C., 2019. Dynamic touch reduces physiological arousal in preterm infants: A role for c-tactile afferents? Dev. Cogn. Neurosci. 39, 100703 https://doi.org/10.1016/J.DCN.2019.100703.

Master, S.L., Eisenberger, N.I., Taylor, S.E., Naliboff, B.D., Shirinyan, D., Lieberman, M. D., 2009. A picture's worth: partner photographs reduce experimentally induced pain. Psychol. Sci. 20 (11), 1316–1318. https://doi.org/10.1111/j.1467-9280.2009.02444.x.

McCabe, C., Rolls, E.T., Bilderbeck, A., McGlone, F., 2008. Cognitive influences on the affective representation of touch and the sight of touch in the human brain. Soc. Cogn. Affect. Neurosci. 3 (2), 97–108. https://doi.org/10.1093/scan/nsn005.

Mcglone, F., Olausson, H., Boyle, J.A., Jones-Gotman, M., Dancer, C., Guest, S., Essick, G., 2012. Touching and feeling: differences in pleasant touch processing between glabrous and hairy skin in humans. Eur. J. Neurosci. 35 (11), 1782–1788. https://doi.org/10.1111/j.1460-9568.2012.08092.x.

McGlone, F., Vallbo, A.B., Olausson, H., Loken, L., Wessberg, J., 2007. Discriminative touch and emotional touch. Can. J. Exp. Psychol. 61 (3), 173–183. https://doi.org/10.1037/cjep2007019.
Meerwijk, E.L., Ford, J.M., Weiss, S.J., 2013. Brain regions associated with psychological pain: implications for a neural network and its relationship to physical pain. Brain Imaging Behav. 7 (1), 1–14. https://doi.org/10.1007/s11682-012-9179-y.
Melzack, R., 1996. Gate control theory: on the evolution of pain concepts. Pain Forum 5 (2), 128–138. https://doi.org/10.1016/S1082-3174(96)80050-X.
Miller, J.G., Vrtička, P., Cui, X., Shrestha, S., Hosseini, S.M.H., Baker, J.M., Reiss, A.L., 2019. Inter-brain synchrony in mother-child dyads during cooperation: an fNIRS hyperscanning study. Neuropsychologia 124, 117–124. https://doi.org/10.1016/j.neuropsychologia.2018.12.021.
Moon, J.-S., Cho, K.-S., 2001. The effects of handholding on anxiety in cataract surgery patients under local anaesthesia. J. Adv. Nurs. 35 (3), 407–415. https://doi.org/10.1046/J.1365-2648.2001.01855.X.
Morelli, S.A., Torre, J.B., Eisenberger, N.I., 2014. The neural bases of feeling understood and not understood. Soc. Cogn. Affect. Neurosci. 9 (12), 1890–1896. https://doi.org/10.1093/scan/nst191.
Morese, R., Lamm, C., Bosco, F.M., Valentini, M.C., Silani, G., 2019. Social support modulates the neural correlates underlying social exclusion. Soc. Cogn. Affect. Neurosci. 14 (6), 633–643. https://doi.org/10.1093/SCAN/NSZ033.
Morrison, I., 2016. Keep calm and cuddle on: social touch as a stress buffer. Adapt. Human Behav. Physiol. 2 (4), 344–362. https://doi.org/10.1007/S40750-016-0052-X.
Morrison, I., Löken, L.S., Minde, J., Wessberg, J., Perini, I., Nennesmo, I., Olausson, H., 2011. Reduced C-afferent fibre density affects perceived pleasantness and empathy for touch. Brain 134 (4), 1116–1126. https://doi.org/10.1093/brain/awr011.
Murray, R.J., Debbané, M., Fox, P.T., Bzdok, D., Eickhoff, S.B., 2015. Functional connectivity mapping of regions associated with self- and other-processing. Hum. Brain Mapp. 36 (4), 1304–1324. https://doi.org/10.1002/HBM.22703.
Nelson, E.E., Panksepp, J., 1998. Brain substrates of infant-mother attachment: contributions of opioids, oxytocin, and norepinephrine. Neurosci. Biobehav. Rev. 22 (3), 437–452. https://doi.org/10.1016/S0149-7634(97)00052-3.
Nguyen, T., Bánki, A., Markova, G., Hoehl, S., 2020. Studying parent-child interaction with hyperscanning. Prog. Brain Res. 254, 1–24. https://doi.org/10.1016/bs.pbr.2020.05.003. Elsevier B.V.
Nummenmaa, L., Tuominen, L., Dunbar, R., Hirvonen, J., Manninen, S., Arponen, E., Machin, A., Hari, R., Jääskeläinen, I.P., Sams, M., 2016. Social touch modulates endogenous μ-opioid system activity in humans. NeuroImage 138, 242–247. https://doi.org/10.1016/j.neuroimage.2016.05.063.
Ochsner, K.N., Barrett, L.F., 2001. A multiprocess perspective on the neuroscience of emotion. Emotions: Currrent Issues and Future Directions. https://doi.org/10.1017/CBO9781107415324.004.
Olausson, H., Wessberg, J., Morrison, I., McGlone, F., Vallbo, Å., 2010. The neurophysiology of unmyelinated tactile afferents. Neurosci. Biobehav. Rev. 34 (2), 185–191. https://doi.org/10.1016/j.neubiorev.2008.09.011. Pergamon.
Osaka, N., Minamoto, T., Yaoi, K., Azuma, M., Shimada, Y.M., Osaka, M., 2015. How two brains make one synchronized mind in the inferior frontal cortex: fNIRS-Based hyperscanning during cooperative singing. Front. Psychol. 6 (November), 1811. https://doi.org/10.3389/fpsyg.2015.01811.
Panksepp, J., 1998. Affective Neuroscience: the Foundations of Human and Animal Emotions - Jaak Panksepp - Google Books. https://books.google.co.il/books?hl=en&lr=&id=qqcRGagyEuAC&oi=fnd&pg=PR13&dq=Panksepp,+J.+(1998).+Affective+neuroscience:+The+foundations+of+human+and+animal+emotions,+Oxford+University+Press.&ots=-PG323AfuB&sig=nqswZlH-B0T_oR6DgJOMqdjddVU&redir_esc=y#v=o.
Peled-Avron, L., Goldstein, P., Yellinek, S., Weissman-Fogel, I., Shamay-Tsoory, S.G., 2018. Empathy during consoling touch is modulated by mu-rhythm: an EEG study. Neuropsychologia 116, 68–74. https://doi.org/10.1016/j.neuropsychologia.2017.04.026.
Ploghaus, A., Tracey, I., Gati, J.S., Clare, S., Menon, R.S., Matthews, P.M., Rawlins, J.N.P., 1999. Dissociating pain from its anticipation in the human brain. Science 284 (5422), 1979–1981. https://doi.org/10.1126/science.284.5422.1979.
Ramseyer, F., Tschacher, W., 2011. Nonverbal synchrony in psychotherapy: coordinated body movement reflects relationship quality and outcome. J. Consult. Clin. Psychol. 79 (3), 284–295. https://doi.org/10.1037/a0023419.
Reddan, M.C., Young, H., Falkner, J., López-Solà, M., Wager, T.D., 2020. Touch and social support influence interpersonal synchrony and pain. Soc. Cogn. Affect. Neurosci. 15 (10), 1064–1075. https://doi.org/10.1093/scan/nsaa048.
Rescorla, R.A., Wagner, A.R., 1972. A theory of pavlovian conditioning : variations in the effectiveness of reinforcement and nonreinforcement. In: Black, A., Prokasy, W.F. (Eds.), Classical Conditioning II: Current Research and Theory. Appleton-Century-Crofts, pp. 64–99.
Rizzolatti, G., Sinigaglia, C., 2016. The mirror mechanism: a basic principle of brain function. Nat. Rev. Neurosci. 17 (12), 757–765. https://doi.org/10.1038/nrn.2016.135.
Rolls, E.T., O'Doherty, J., K, M.L., F, S., Bowtell, R., McGlone, F., 2003. Representations of pleasant and painful touch in the human orbitofrontal and cingulate cortices. Cereb. Cortex 13 (3), 308–317. https://doi.org/10.1093/cercor/13.3.308.
Romero, T., Castellanos, M.A., De Waal, F.B.M., 2010. Consolation as possible expression of sympathetic concern among chimpanzees. Proc. Natl. Acad. Sci. U. S. A. 107 (27), 12110–12115. https://doi.org/10.1073/pnas.1006991107.
Romero, T., Castellanos, M.A., de Waal, F.B.M., 2011. Post-conflict affiliation by chimpanzees with aggressors: other-oriented versus selfish political strategy. PLoS One 6 (7), e22173. https://doi.org/10.1371/journal.pone.0022173.
Roy, M., Peretz, I., Rainville, P., 2008. Emotional valence contributes to music-induced analgesia. Pain 134 (1–2), 140–147. https://doi.org/10.1016/j.pain.2007.04.003.
Sahi, R.S., Dieffenbach, M.C., Gan, S., Lee, M., Hazlett, L.I., Burns, S.M., Lieberman, M.D., Shamay-Tsoory, S.G., Eisenberger, N.I., 2021. The comfort in touch: immediate and lasting effects of handholding on emotional pain. PLoS One 16 (2), e0246753. https://doi.org/10.1371/JOURNAL.PONE.0246753.
Sailer, Triscoli, U., Häggblad, C.G., Hamilton Olausson, P.H., Croy, I., 2016. Temporal dynamics of brain activation during 40 minutes of pleasant touch. NeuroImage 139 (1), 360–367.
Sambo, C.F., Howard, M., Kopelman, M., Williams, S., Fotopoulou, A., 2010. Knowing you care: effects of perceived empathy and attachment style on pain perception. PAIN 151 (3), 687–693. https://doi.org/10.1016/J.PAIN.2010.08.035.
Scalabrini, A., Huang, Z., Mucci, C., Perrucci, M.G., Ferretti, A., Fossati, A., Romani, G.L., Northoff, G., Ebisch, S.J.H., 2017. How spontaneous brain activity and narcissistic features shape social interaction. Sci. Rep. 7 (1), 1–12. https://doi.org/10.1038/s41598-017-10389-9.
Scalabrini, A., Ebisch, S.J.H., Huang, Z., Di Plinio, S., Perrucci, M.G., Romani, G.L., Mucci, C., Northoff, G., 2019. Spontaneous brain activity predicts task-evoked activity during animate versus inanimate touch. Cereb. Cortex 29 (11), 4628–4645. https://doi.org/10.1093/CERCOR/BHY340.
Scott, D.J., Stohler, C.S., Egnatuk, C.M., Wang, H., Koeppe, R.A., Zubieta, J.K., 2008. Placebo and nocebo effects are defined by opposite opioid and dopaminergic responses. Arch. Gen. Psychiatry 65 (2), 220–231. https://doi.org/10.1001/archgenpsychiatry.2007.34.
Seed, A.M., Clayton, N.S., Emery, N.J., 2007. Postconflict third-party affiliation in Rooks, Corvus frugilegus. Curr. Biol. 17 (2), 152–158. https://doi.org/10.1016/j.cub.2006.11.025.
Seehausen, M., Kazzer, P., Bajbouj, M., Prehn, K., 2012. Effects of empathic paraphrasing – extrinsic emotion regulation in social conflict. Front. Psychol. 3 (November), 482. https://doi.org/10.3389/fpsyg.2012.00482.
Shamay-Tsoory, S.G., 2011. The neural bases for empathy. Neuroscientist 17 (1), 18–24. https://doi.org/10.1177/1073858410379268.
Shamay-Tsoory, S., Saporta, N., Marton-Alper, I.Z., Gvirts, H.Z., 2019. Herding brains: a core neural mechanism for social alignment. Trends Cogn. Sci. (Regul. Ed.) 23 (3), 174–186.
Sharma, S., Fiave, P.A., Nelissen, K., 2018. Functional MRI responses to passive, active, and observed touch in somatosensory and insular cortices of the macaque monkey. J. Neurosci. 38 (15), 3689–3707. https://doi.org/10.1523/JNEUROSCI.1587-17.2018.
Silva, L., Schalock, M., 2016. First skin biopsy reports in children with autism show loss of C-Tactile fibers. J. Neurol. Disord. 4 (626), 4. https://doi.org/10.4172/2329-6895.1000262.
Sorokowska, A., Saluja, S., Sorokowski, P., Frąckowiak, T., Karwowski, M., Aavik, T., Akello, G., Alm, C., Amjad, N., Anjum, A., Asao, K., Atama, C.S., Duyar, D.A., Ayebare, R., Batres, C., Bendixen, M., Bensafia, A., Bizumic, B., Boussena, M., et al., 2021. Affective interpersonal touch in close relationships: a cross-cultural perspective. Pers. Soc. Psychol. Bull. 8 https://doi.org/10.1177/0146167220988373, 0146167220988373.
Spratling, M.W., 2017. A review of predictive coding algorithms. In: Brain and Cognition, 112. Academic Press, pp. 92–97. https://doi.org/10.1016/j.bandc.2015.11.003.
Sutton, R.S., Barto, A.G., 2012. Vol. 1. Reinforcement Learning: an Introduction, 2nd ed. MIT press. https://doi.org/10.1109/MED.2013.6608833. Issue 1.
Suvilehto, J.T., Glerean, E., Dunbar, R.I.M., Hari, R., Nummenmaa, L., 2015. Erratum: Topography of social touching depends on emotional bonds between humans (Proceedings of the National Academy of Sciences of the United States of America (2015) 112:45 (13811-13816) (10.1073/pnas.1519231112)). Proc. Natl. Acad. Sci. U. S. A. 112 (48), E6718. https://doi.org/10.1073/pnas.1521810112.
Tamir, D.I., Thornton, M.A., 2018. Modeling the predictive social mind. Trends Cogn. Sci. (Regul. Ed.) 22 (3), 201–212. https://doi.org/10.1016/j.tics.2017.12.005.
Tang, Y., Benusiglio, D., Lefevre, A., Hilfiger, L., Althammer, F., Bludau, A., Hagiwara, D., Baudon, A., Darbon, P., Schimmer, J., Kirchner, M.K., Roy, R.K., Wang, S., Eliava, M., Wagner, S., Oberhuber, M., Conzelmann, K.K., Schwarz, M., Stern, J.E., et al., 2020. Social touch promotes interfemale communication via activation of parvocellular oxytocin neurons. Nat. Neurosci. 23 (9), 1125–1137. https://doi.org/10.1038/s41593-020-0674-y.
Triscoli, C., Croy, I., Olausson, H., Sailer, U., 2017. Touch between romantic partners: being stroked is more pleasant than stroking and decelerates heart rate. Physiol. Behav. 177, 169–175. https://doi.org/10.1016/J.PHYSBEH.2017.05.006.
Urry, H.L., 2010. Seeing, thinking, and feeling: emotion-regulating effects of gaze-directed cognitive reappraisal. Emotion 10 (1), 125–135. https://doi.org/10.1037/a0017434.
Vachon-Presseau, E., 2018. Effects of stress on the corticolimbic system: implications for chronic pain. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 87 (Part B), 216–223, 20 December 2018.
Vallbo, A.B., Johansson, R.S., 1984. Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. Hum. Neurobiol. 3, 3–14.
Van Puyvelde, M., Gorissen, A.S., Pattyn, N., McGlone, F., 2019. Does touch matter? The impact of stroking versus non-stroking maternal touch on cardio-respiratory processes in mothers and infants. Physiol. Behav. 207, 55–63. https://doi.org/10.1016/J.PHYSBEH.2019.04.024.
Vogt, B.A., 2005. Pain and emotion interactions in subregions of the cingulate gyrus. Nat. Rev. Neurosci. 6 (7), 533–544. https://doi.org/10.1038/nrn1704. Nature Publishing Group.
von Mohr, M., Fotopoulou, A., 2018. Of Interoception: Active and Social Inference of Pain and Pleasure on. In the Interoceptive Mind: From Homeostasis to Awareness. https://books.google.co.il/books?hl=en&lr=&id=o0VvDwAAQBAJ&oi=fnd&p

g=PA102&dq=von+Mohr,+M.+and+A.+Fotopoulou,+of+interoception:+Active+and+social+inference+of+pain+and+pleasure+on.+The+interoceptive+mind:+From+homeostasis+to+awareness,+2018.+102&ots=RIW_g.

von Mohr, Mariana, Krahé, C., Beck, B., Fotopoulou, A., 2018. The social buffering of pain by affective touch: a laser-evoked potential study in romantic couples. Soc. Cogn. Affect. Neurosci. 13 (11), 1121–1130. https://doi.org/10.1093/scan/nsy085.

Wager, T.D., van Ast, V.A., Hughes, B.L., Davidson, M.L., Lindquist, M.A., Ochsner, K.N., 2009. Brain mediators of cardiovascular responses to social threat, Part II: prefrontal-subcortical pathways and relationship with anxiety. NeuroImage 47 (3), 836–851. https://doi.org/10.1016/j.neuroimage.2009.05.044.

Wager, T.D., Atlas, L.Y., Lindquist, M.A., Roy, M., Woo, C.-W., Kross, E., 2013. An fMRI-Based neurologic signature of physical pain. N. Engl. J. Med. 368 (15), 1388–1397. https://doi.org/10.1056/nejmoa1204471.

Walker, S.C., Trotter, P.D., Swaney, W.T., Marshall, A., Mcglone, F.P., 2017. C-tactile afferents: cutaneous mediators of oxytocin release during affiliative tactile interactions?. In: Neuropeptides, Vol. 64 Churchill Livingstone, pp. 27–38. https://doi.org/10.1016/j.npep.2017.01.001.

Weekes, D.P., Kagan, S.H., James, K., Seboni, N., 1993. The phenomenon of hand holding as a coping strategy in adolescents experiencing treatment-related pain. J. Pediatr. Oncol. Nurs. 10 (1), 19–25. https://doi.org/10.1177/104345429301000105.

Wolpert, D., Ghahramani, Z., Jordan, M., 1995. An internal model for sensorimotor integration. Science 269 (5232), 1880–1882. https://doi.org/10.1126/science.7569931.

Yaniv, A.U., Salomon, R., Waidergoren, S., Shimon-Raz, O., Djalovski, A., Feldman, R., 2021. Synchronous caregiving from birth to adulthood tunes humans' social brain. Proc. Natl. Acad. Sci. 118 (14) https://doi.org/10.1073/PNAS.2012900118.

Zaki, J., Bolger, N., Ochsner, K., 2008. It takes two: the interpersonal nature of empathic accuracy. Assoc. Psychol. Sci. 19 (4), 399–404. https://doi.org/10.5840/faithphil200219441.

Zhang, Y., Meng, T., Hou, Y., Pan, Y., Hu, Y., 2018. Interpersonal brain synchronization associated with working alliance during psychological counseling. Psych. Res. - Neuroimaging 282, 103–109. https://doi.org/10.1016/j.pscychresns.2018.09.007.