Hedonic, neural, and autonomic responses to prolonged gentle touch

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Chantal Triscoli

Department of Psychology
University of Gothenburg
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Department of Psychology
University of Gothenburg
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chantal.triscoli@psy.gu.se
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Ai miei genitori
Nicoletta e Roberto

Abstract

Physical contact among individuals, such as caressing and cuddling, is connoted by a strong emotional value, and is usually perceived as a pleasant and rewarding experience. C tactile (CT) afferents are a class of fibres that are specific channels for detecting touch at a caress-like velocity (between 1 and 10 cm/s). This velocity usually occurs during social interactions and is perceived as pleasant. Alongside rich literature about short-lasting pleasant touch, the aim of the present thesis is to increase the knowledge of the neural and physiological dynamics of pleasant touch performed for time scales longer than several minutes.

In paper I, handheld and robotic brush strokes were compared in terms of pleasantness in order to validate the use of a robot for delivering the tactile stimulation in the prolonged touch paradigms used in papers II, III and IV. Moreover, the influence of a cognitive factor such as the awareness of the source of the stimulation on the evaluation of pleasant touch was investigated. Brush stroking was applied on the forearm either manually or with a robot, and the participants were either aware or unaware of the source. The results showed that robot and human touch were equally pleasant, proving the convergent validity of the two measures. This was also true regardless of the awareness of the source, meaning that, in the present context, there was no strong cognitive modulation on the perception of pleasant touch

In paper II, in a prolonged touch paradigm, the concept of “satiety for touch” and the rewarding aspects of “liking” (pleasantness) and “wanting” (willingness to be exposed again to the same stimulus) were investigated , with both velocity variation (experiment I) and one single velocity (experiment II). In experiment I, “liking” and “wanting” decreased only for the velocity optimally activating CT afferents (3 cm/s), but the stimulation was still pleasant at the end. In experiment II, “liking” and “wanting” decreased for both stroking at 3 and 30 cm/s, with a steeper decrease for 3 cm/s. These findings indicate that “satiety” occurs particularly for the CT optimal velocity; however it takes time.

Paper III investigated the neural response to prolonged CT optimal touch. Forty minutes of brush stroking was performed while the participants were scanned with functional Magnetic Resonance Imaging (fMRI). Whole brain-based analyses showed decreased activation over time of primary and secondary somatosensory cortices (SI and SII), and increased activation in orbitofrontal cortex (OFC) and putamen. OFC activation was correlated with the perceived pleasantness, which decreased over time although never below the neutral point. The results demonstrate that long-lasting stroking is processed in similar areas to shorter-lasting stroking, and that the recruitment of the reward-related orbitofrontal network likely reflects updating of the rewarding value of touch.

In paper IV we explored the psychological and physiological effects of either 35 minutes of brush stroking at the CT optimal velocity or vibration on stress response, reward sensitivity, current mood and interoceptive awareness. The perceived pleasantness decreased for both groups, while intensity remained stable. The increase in heart rate variability (SDNN) observed exclusively for brush stroking was related to its higher pleasantness and intensity compared to vibration. No significant changes in the other variables were found. The findings demonstrate the potential of prolonged CT-optimal touch in improving autonomic regulation.

This thesis contributes to the growing field of affective touch by demonstrating that prolonged CT optimal touch is a pleasant experience processed by the reward-related neural network, which provides positive autonomic effects. As well, in the present context, pleasant touch was not affected by the source of the stimulation nor by the awareness of it. These findings may be relevant for situations of prolonged touch such as touch therapies and massages, in order to increase the well-being of the individuals.

Keywords: long-lasting touch, CT afferents, pleasantness, liking, wanting, satiety, orbitofrontal cortex, reward, heart rate variability

Svensk sammanfattning

Behaglig beröring är en hedonisk upplevelse och ett kraftfullt sätt att skapa och upprätthålla en nära relation med en annan person. Smekningsliknande beröring detekteras av C taktila (CT) fibrer, en sorts låg-tröskliga, omyeliniserade och långsamt ledande mekanoreceptorer som endast finns i hårig hud på kroppen. Tidigare studier har visat att dessa nervfibrer aktiveras optimalt när huden borstas försiktigt med en hastighet som motsvarar en smekning (mellan 1 cm/s och 10 cm/s). Man har även visat att borstningar med denna hastighet uppfattas som mest behagliga. Som komplettering av den redan existerande litteraturen om kortvarig behaglig beröring, så är syftet med denna avhandling att öka kunskapen om den kognitiva, neurala och fysiologiska effekten av behaglig beröring utförd under längre tid.

Syftet med delarbete I var att avgöra om handhållen eller mekanisk producerade borstningar utvärderas lika med avseende på upplevt behag. Det undersöktes även om top-down faktorer såsom vetskap om källan av stimuleringen kan påverka den subjektiva bedömningen av behag. Deltagarna borstades med en mjuk pensel på underarmen med tre olika hastigheter (0.3 cm/s, 3 cm/s och 30 cm/s), antingen handhållet (av en människa) eller mekaniskt (av en robot). Hälften av deltagarna var medvetna om källan av stimuleringen, de andra inte. Deltagarna skattade det upplevda behaget och intensiteten för varje stimulering. Skattningen var likartad oavsett vetskap om källan. CT optimerade borstningar uppfattades som behagligast. För de två långsammare hastigheterna (0.3 cm/s och 3 cm/s) var intensitetsskattningen högre under de handhållna villkoren. Dessa resultat visar att ”top-down” faktorer, d.v.s. vetskapen om vem eller vad som genererar borstningen, inte påverkar bedömningen av behag i detta sammanhang. Resultaten visar också hög jämförbarhet mellan borststimulering gjord av människa och robot. Detta validerar vår metod att använda en robot som taktil stimulator, vilket möjliggör konstant och exakt replikering av både hastighet och kraft av taktil stimulering över en lång exponering, vilket är en förutsättning för delarbete II, III och IV.

I delarbete II undersöktes om det upplevda taktila behaget ändrades med repetitiv exponering, vilket skulle leda till ”mättnad”, samt om detta varierade med olika hastigheter. Även belöningskomponenterna av "liking" (hedonisk utvärdering av stimuleringen) och "wanting" (att vilja ha samma stimulering igen) för beröring utvärderades. Borstdrag levererades på underarmen i ca 50 minuter, i experiment I med tre olika hastigheter (0,3 cm/s, 3 cm/s och 30 cm/s) och i experiment II med en hastighet (antingen 3 cm/s eller 30 cm/s). Efter varje borstning fick deltagarna betygsätta taktil upplevelse i form av "liking" och "wanting". Experiment I visade en liten minskning i både "liking" och "wanting" enbart för CT optimerade borststimulering (hastigheten 3 cm/s). Stimuleringen upplevdes aldrig som obehaglig. Experiment II visade en minskning i "liking" och "wanting" för båda hastigheterna, men enbart "liking" för hastigheten 3 cm/s hamnade i det negativa/obehagliga intervallet. ”Mättnad” har definierats som ett fenomen som inträffar när stimulansen blir obehaglig. Med tanke på detta skulle resultaten tyda på att välbehaget kvarstår länge och att "mättnad" för beröring sker enbart för smekningsliknande CT optimerade borstning. Detta tar dock tid, mer än 50 minuter. Mättnad för beröring kan troligen ta ännu längre tid i vardagliga situationer, där smekningsliknande interaktioner varierar i typ, hastighet och riktning. I delarbete III, undersökte vi de neurala effekterna av långvarig beröring genomfört med CT-optimerad borstningshastighet. Deltagarna borstades under 40 minuter samtidigt som de undersöktes med funktionell magnetisk resonansavbildning (fMRI). Deltagarna betygsatte behaget av den taktila upplevelsen. Analyser av hela hjärnan visade minskad aktivering över tid av primära, (SI) och sekundära, (SII) somatosensoriska kortex. Ökad aktivering sågs i orbitofrontal cortex (OFC) och putamen under den första hälften av borststimuleringen (ca 20 minuter) och under den senare delen skedde ingen förändring. Aktivering i OFC korrelerades med den upplevda behagligheten, som minskade under den första hälften av experimentet (beröringen blev aldrig obehaglig) och ingen förändring skedde under den senare delen av experimentet. Vid slutet av experimentet observerades funktionell konnektivitet mellan bakre insula och belöningsrelaterade regioner som putamen och nucleus caudatus. Under hela experimentet samvarierade bakre insula med somatosensoriska regioner bilateralt i hjärnan. Resultaten visar att långvarig beröring bearbetas i liknande neurala regioner som kortvarig beröring, och att rekryteringen av det orbitofrontala nätverket troligen registrerar förändringarna av det hedoniska värdet av beröring.

Delarbete IV undersökte de psykologiska och fysiologiska effekterna av antingen CT optimerad borstning eller vibrationer, d.v.s. stressrespons (kortisol nivå, hjärtfrekvensvariation och ett frågeformulär), belöningskänslighet, nuvarande humör, ”interoceptiv” medvetenhet och taktil känslighet. Stimuleringen pågick under 35 minuter. Deltagarna betygsatte hur behaglig och intensiv den taktila stimuleringen var. Den upplevda behagligheten minskade för båda grupperna, medan intensiteten var stabil under hela försöket. En ökning av hjärtfrekvensvariationen observerades enbart för borstning och var relaterad till mer välbehag och högre intensitet jämfört med vibration. Kortisolnivån minskade för både CT optimerad borstning och vibration. Ingen signifikant effekt hittades för de andra variablerna. Resultaten visar att långvarig CT-optimerad beröring kan förbättra det fysiologiska välbefinnandet.

Denna avhandling bidrar till den växande kunskapen om behaglig beröring då den visar att långvarig CT-optimal beröring har ett belöningsvärde som kvarstår länge, bearbetas av liknande neurala nätverk som kortvarig beröring (d.v.s. belöningsrelaterade neurala nätverket) och ger positiva autonoma effekter på individernas välbehag, vilket visades av ökad hjärtfrekvensvariation. Dessutom visades att det upplevda behaget av beröring är robust mot kognitiva faktorer såsom vetskap om källan av den taktila stimuleringen. Dessa resultat kan vara relevanta i situationer med långvarig beröring, såsom beröringsterapi och massage, för att öka individernas välbefinnande.

List of papers

This thesis consists of a summary and the following four papers, which are referred to by their Roman numerals:

I. **Triscoli, C.**, Olausson, H., Sailer, U., Ignell, H., Croy, I.

CT-optimized skin stroking delivered by hand or robot is comparable.

Frontiers in Behavioural Neuroscience 2013: 7(208).

doi:10.3389/FNBEH.2013.00208

II. **Triscoli, C.**, Ackerley, R., Sailer, U.

Touch satiety: differential effects of stroking velocity on liking and wanting touch over repetitions.

PlosOne 2014: 9(11), E113425.

doi:10.1371/JOURNAL.PONE.0113425

III. Sailer, U., **Triscoli, C.,** Häggblad, G., Hamilton, P., Olausson, H., Croy, I.

Temporal dynamics of brain activation during 40 minutes of pleasant touch.

Neuroimage 2016: 139, 360-367.

doi:10.1016/J.NEUROIMAGE.2016.06.031

IV. **Triscoli, C.**, Croy, I., Steudte-Schmiedgen, S., Olausson, H., Sailer, U.

Heart rate variability is enhanced by long-lasting pleasant touch at CT-optimized velocity.

Biological Psychology 2017: 128, 71–81.

doi.org/10.1016/j.biopsycho.2017.07.007

Contents

List of abbreviations

AUCG – area under the curve with respect to the ground

AUCI –area under the curve with respect to the increase

BDI-II – Beck depression inventory-II

BIS/BAS – behavioural inhibition and activation systems scale

BOLD – blood oxygen level dependent

CT – C tactile

C-LTMR – C low threshold mechanosensitive receptor

fMRI – functional magnetic resonance imaging

FC – functional connectivity

HRV – heart rate variability

LMM – linear mixed model analysis

LTS – linear tactile stimulator

MANOVA – multivariate analysis of variance

MDMQ – multidimensional mood state questionnaire

OFC – orbitofrontal cortex

PANAS – subjective measure of positive affect and negative affect scale

pgACC – pregenual anterior cingulate cortex

RTS – rotary tactile stimulator

SI – primary somatosensory cortex

SII – secondary somatosensory cortex

SDNN – standard deviation of normal to normal inter-beat intervals

STS – superior temporal sulcus

TEPS – temporal experience of pleasure scale

VAS – visual analogue scale

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1. Introduction

Close affiliative interactions among individuals can involve forms of slow, gentle stimulation such as stroking and massaging. Such “affective touch” may constitute a specific domain of touch, distinct from other tactile sensation and characterized by its social, pleasant and subjective component. In these terms, affective touch is likely to signal close, affiliative body contact with others (Olausson et al., 2010). Furthermore, it is usually performed in order to provide feelings of affection, security, and demonstration of positive attention (Gallace & Spence, 2010).

There is reason to believe that affective touch has a critical role in creating and facilitating affiliative behaviours and social bonding (McGlone, Wessberg, & Olausson, 2014; Morrison, Löken, & Olausson, 2010). Besides such hedonic and “social” features, tender tactile interactions among individuals are seen to provide calming physiological effects (Drescher, Whitehead, Morrill-Corbin, & Cataldo, 1985), as well as to be of critical help in handling stressful circumstances (Ditzen et al., 2007; Grewen, Anderson, Girdler, & Light, 2003; Olson & Sneed, 1995). A fundamental distinction into the domain of touch can be made between its discriminative and affective dimensions, which perceptually can be denoted as “sensing” (discrimination) and “feeling” (affect) (McGlone, Wessberg, & Olausson, 2014). The role of the discriminative tactile system is to encode with high precision the temporal and spatial properties of a tactile stimulus, for example what, when and where it is happening on the skin. This sensory dimension allows the perception of critical information such as texture, force and velocity (Olausson et al., 2010; Vallbo & Johansson, 1984), required during exploratory behaviours, object manipulation and control of muscle actions (McGlone, Wessberg, & Olausson, 2014). On the other hand, the affective tactile system encodes the emotional and hedonic experience of touch. These dimensions of touch are important for providing feelings of pleasure, closeness to a friend, comfort, and security (Morrison et al, 2010), as well as in expressing emotional support, intimacy and tenderness (Jones & Yarbrough, 1985; Register & Henley, 1992). A gentle caress provided by a loved one is likely to arouse pleasant emotions, and human touch in general establishes a sense of proximity and human connection (Montagu & Matson, 1979).

1.1 Peripheral signalling of touch

The human tactile system can be divided already at a peripheral receptor level, i.e. at the level of primary afferents, into a fast and a slow system that differ in conduction velocity. The tactile afferents involved in detecting the discriminative aspects of touch are the fast-conducting (30 – 75 m/s), myelinated, low-threshold Aβ mechanoreceptors (Vallbo & Johansson, 1984). Historically, the large myelinated Aβ afferents were considered to be the only afferents that carried human non-nociceptive tactile information. However, the discovery of slow conducting, unmyelinated afferents C-LTMR (C low threshold mechanosensitive receptors) in furry animals, first observed in the hairy skin of the cat by the Swedish physiologist Zotterman in 1939, provided the first evidence of the dual nature of the tactile system (Zotterman, 1939). His initial hypothesis was that such unmyelinated slow system accounted for tickling sensations. However, later observations demonstrated that tickling is rather underpinned by the large Aβ afferents (Cole et al., 2006). For some time after this discovery, the slow tactile system was thought to be lacking in man, probably due to evolutionary processes (Kumazawa and Perl, 1977). However, microneurography studies (axonal nerve recordings from single afferents in awake humans) (Hagbarth and Vallbo, 1968) eventually led to the observation of a class of slowly conducting (~1 m/s), low-threshold, unmyelinated mechanoreceptors, also present in the hairy skin of the human body (Nordin, 1990; Vallbo et al., 1993; Löken et al., 2009). Such discovery provided the first evidence of a different tactile pathway, called C tactile (CT) system, probably involved in detecting the affective aspects of touch (Olausson, Wessberg, Morrison, McGlone, & Vallbo, 2010; Olausson et al., 2008). As opposed to the Aβ afferents, the CT afferents have only been encountered in recordings from the human hairy skin of the body, but never from the glabrous (not hairy) skin of palms and soles (Ackerley et al., 2014b; Liljencrantz & Olausson, 2014). The (abundant) presence of the fast conducting Aβ afferents on the glabrous skin of the human body might have functional benefits, as that of preserving primary vital roles like object discrimination (palms) and walking and running (soles) (Löken et al., 2011).

1.2 Properties of the CT afferents

Interestingly, the CT afferents show stroking velocity dependence, with optimal firing frequencies recorded with gentle stimuli such as brush stroking within the range of 1 – 10 cm/s, i.e. a velocity that corresponds the most closely to a human caress and is also perceived as particularly pleasant. CT afferents respond less vigorously to slower or faster velocities (Löken et al., 2009). The curvilinear (inverted U shaped) relationship seen between CT firing and velocity is not seen for the Aβ afferents, whose firing frequencies increase with the velocity of the stroking. Similarly to the Aβ afferents, the CT afferents respond to skin deformation at a force range of 0.3–2.5 mN (Vallbo, 1999). The subjective feelings of pleasantness show the same velocity dependence as the firing rates of the CT afferents. More specifically, stroking velocity and hedonic ratings are described by an inverted U shape relationship, with higher perceived pleasantness for the velocity of 3 cm/s, and lower ratings for slower or faster velocities (Löken et al., 2009; Essick et al., 1999). This observation further supports the notion that the CT system is important for the hedonic perception and evaluation of affective touch. Conversely, subjective ratings of intensity show a linear relationship with the stroking velocity, meaning that they increase with the velocity of the tactile stimulation in a similar way to the Aβ firing (Löken et al., 2009). The higher the activation of the Aβ afferents, the more intense the touch is perceived.

Another feature of the CT afferents is that they have an optimal thermal range, with highest firing frequencies found for tactile stimuli delivered at normal skin temperature (32° C), while they respond less vigorously to warmer or cooler temperatures (Ackerley et al., 2014a). Further, the curvilinear relationship between CT firing and subjective estimates of pleasantness is highly significant only at normal skin temperatures (Ackerley et al., 2014a). Such effects have not been seen for the Aβ afferents, further supporting the notion that the CT afferents are specialized for encoding touch with the characteristics of a typical human caress.

The CT afferents are easily fatigued, and may stop firing as soon as after about four seconds of tactile stimulation (Wiklund Fernstrom et al., 2002). This phenomenon occurs when the CT afferents, continuously stimulated, reduce their firing during the ongoing tactile stimulation (Nordin, 1990; Olausson et al., 2002). Therefore, one may assume that a potential decrease in pleasantness for touch depends upon the reduced CT firing due to fatigue. Recordings in the cat showed that CT afferents have a slow recovery, and full restoration can take several (4-30) minutes (Iggo, 1960). This means that this class of fibres might be more responsive to an initial touch than to subsequent stimulation. Therefore, we might appreciate a gentle caress more when it is first received than when prolonged for a long time. In these terms, in paper II we investigated how pleasantness for touch (termed “liking”) as well as the willingness to be touched again (termed “wanting”) developed over a prolonged period of tactile stimulation. At the receptor level, it can be speculated that a potential decrease in the perceived pleasantness to repetitive touch at 3 cm/s velocity may be related to the decreased activity of the CT afferents.

1.3 Robotic versus human brush stroking

Taken into consideration the prerequisite of paper II, III and IV, i.e. a robotic long-lasting tactile stimulation performed for more than 30 minutes, it is of our primary interest to determine in **Paper I** whether robotic brush strokes are perceived as equally pleasant as brush strokes applied by hand. If this is the case, such result would validate our method of using a robot for delivering the stroking in paper II, III and IV. Robotic tactile stimulation is the optimal choice during prolonged touch because it provides a higher degree of precision and constancy of both velocity and force than a human hand. In fact, long-lasting paradigms demand exact and rigidly controlled parameters for a rather long time, which are crucial factors for achieving the force range (0.3–2.5 mN) and velocity (1-10 cm/s) that optimally activate the CT afferents (Ackerley et al., 2014b; Löken et al., 2009; Vallbo et al., 1999) and may be difficult to produce by hand. A handheld brush may not allow a precise replication of the stroking over a long time, this because the performance of the experimenter may be affected by tiredness or muscle fatigue, for example.

Additionally, determining whether robot and handheld stimulations are comparable in terms of pleasantness would enable the investigation of the convergent validity of robotic and handheld brush stroking. As well, such an investigation would allow the application of handheld tactile stimulation in situations where a robotic source is not available or applicable, such as with small body parts or with a tight budget.

An additional important aim of **Paper I** was to understand whether and how the bottom up input produced by touch conveyed by the CT afferents at the peripheral receptor level is linked to top down processes. On this line of inquiry, in paper I we manipulated the awareness of the source of the tactile stimulation, i.e. in one condition the participants were aware whether they were brush-stroked by a robot or by the experimenter, while in the other condition they were not. Specifically, it was of interest to investigate whether the perceived pleasantness of affective touch is influenced by the knowledge of the source of the stimulation. A rewarding stimulus such as touch is only rarely a "pure" experience; indeed there can be several contextual and cognitive factors which potentially influence the hedonic evaluation of a stimulus (Lindgren et al., 2014). For example, in certain contexts and societies, touch is judged as shameful and connoted by taboos (Gallace & Spence, 2010); therefore such cognitive factors may limit its hedonic experience.

In general, top down regulation of the affective experience can also be seen in laboratory settings. Participants may show certain behaviours which do not mirror their true intentions, but are adopted with the aim of "pleasing" the experimenter (Grimm, 2010) or in order to obtain a desirable outcome (King & Bruner, 2000). In terms of touch, "social desirability" may for example occur when the participants report the tactile experience as being more pleasant than what it actually is. As well, expectations can cognitively modulate how touch is perceived: for example, the assumed gender of the toucher (Gazzola et al., 2012), or the valence of the labels assigned to the tactile stimulus (McCabe et al., 2008). Specifically, when a cream applied to the forearm is labelled as "rich moisturizing," the related touch is evaluated as more pleasant than when the same type of cream is labelled as "basic." It has also been shown that the judgment of a massage experience can be affected by the mental state of the therapist (Lindgren et al., 2014). Finally, it is worthwhile to cite the "Like me theory." This theory postulates that actions performed by entities similar to the self are rated better than actions performed by entities dissimilar to the self (Meltzoff, 2007). Following this theory, it may be that higher pleasantness ratings occur when the brush strokes are performed by the experimenter (more similar to the self) than when they are delivered by a robotic source (less similar to the self). It must be noted that handheld touch is potentially more affected by top down processes than touch performed by a mechanical source. For example, handheld touch may be influenced by the like or dislike towards the experimenter, therefore the use of a robotic source, if comparable in terms of pleasantness, would reduce this top down influence. Hence, besides reducing variance by keeping constant velocity and force during the tactile stimulation, the use of a robot in paper II, III and IV may also have the advantage of reducing top down effects from the pure CT-related pleasant experience of touch.

1.4 Affective touch as a rewarding experience

Affective touch is a hedonic experience (Olausson et al., 2016). However, a human caress may lose part of its rewarding value when protracted for a very long time, leading to "satiety for touch." Satiety is defined as the phenomenon occurring after repeated exposure to a sensory stimulus, which leads to a decrease in its rewarding properties (Rolls, Rolls, Rowe, & Sweeney, 1981). Hence, a previously rewarding sensory experience is no longer perceived as rewarding after reaching satiety (O'Doherty, 2004). It seems therefore that satiety and the reward value assigned to a stimulus are strictly related concepts. To the best of our knowledge, no previous investigations have looked closely at whether repeated exposure to tactile stimuli over a prolonged period of time leads to "satiety" and how this mechanism evolves. Knowing whether "satiety" for pleasant touch occurs would advance our understanding of the role of touch in social interactions. For instance, it seems possible that brief tactile interactions among individuals could be more rewarding than long-lasting physical contact. Such knowledge would also have implications in other circumstances where long-lasting touch occurs, such as touch therapies and massages (Lindgren et al., 2014), where its beneficial effects are expected.

Touch is usually perceived as pleasant, and it has an intrinsic rewarding value which drives active seeking behaviours (Berridge & Robinson, 2003). This may explain why people seek pleasant tactile stimulations, like being caressed and stroked by a partner or a family member (Suvilehto et al., 2015). In other words, individuals not only *like* touch but they also *want* it. The concept of reward can be distinguished into termed "liking" and "wanting." These can be seen as the two sides of the same coin: intrinsically interrelated (Havermans, 2011), even though psychologically dissociable from each other (Berridge, 2009). On the one side, "liking" relates closely to the notion of pleasure, and corresponds to the emotionally connoted, conscious, and subjective response to the hedonic value of a stimulus. On the other side, "wanting" relates more closely to the motivation or desire of being further exposed to the same rewarding stimulus (Berridge & Robinson, 2003), and it can be triggered unconsciously (Berridge, 2009). For example, in the case of gustatory stimuli, "liking" corresponds to the palatability of the taste of the stimulus, while "wanting" is more linked to the motivational process of appetite that triggers the individual to eat more of the same food (Berridge, 1996) In the domain of touch, "liking" could be defined as the hedonic experience derived from being touched by a close one, while "wanting" might be more related to the wish to be touched. With these aims, in **Paper II** we developed a new paradigm with a rather long exposure to touch, in order to answer the research question whether the rewarding value of affective touch is influenced by the length of the exposure, and thus whether "satiety" for pleasant touch arises at a certain point. The evolution of "liking" and "wanting" touch over time were explored in order to determine whether and how the repeated exposure to pleasant touch changes in terms of perceived pleasantness ("liking") and motivation to be further exposed to the same tactile stimulation again ("wanting"), and whether these two reward aspects can be dissociated from each other. An eventual decrease in "liking" and/or "wanting" during continuous tactile stimulation may lead to the observation that touch is no longer a pleasant experience, or that is no longer desired, after being exposed to it for a long time, and that shorter physical contacts are more rewarding. As well, a potential difference between “liking” and “wanting” may provide evidence that people do not want to be touched anymore after a certain point, even though they may still like touch. Moreover, we investigated whether “satiety” for pleasant touch depends upon the velocity of the stimulation. Paper II was inspired by the concept of “sensory specific satiety”. This phenomenon occurs for the repetitively applied stimulus but not for other stimuli. For example, gustatory sensory specific satiety can be seen in lower pleasantness ratings for the sight of the food eaten to satiety compared to the pleasantness ratings for the sight of other foods (Rolls, Rolls, & Rowe, 1983). As well, the smell of a food eaten to satiety is less pleasant than the smell of other foods which have not been eaten; this phenomenon is called olfactory sensory specific satiety (Rolls & Rolls, 1997). Paper II involved an experiment where three different velocities were equally presented, and a second experiment, where one single stroking velocity was applied.

1.5 Cortical processing of affective touch

CT optimal stimulation such as caress-like stroking also activates the large Aβ afferents, which project to primary (SI) and secondary (SII) somatosensory cortices, therefore it is hard to disentangle and study the specific central projections of affective touch targeting CT afferents. In these terms, neural activation during gentle brush stroking is seen also in SI and SII, dedicated to the actual perception of Aβ-mediated touch (Chapman, 1994; Ploner et al., 2000; Schaefer et al., 2006). However, neuroimaging data from a unique patient, GL, of 31 years old, led to the opportunity to study the specific central projections of CT-mediated affective touch (Olausson et al., 2002). Due to sensory neuropathy, GL has a loss of Aβ myelinated afferents; the CT afferents, however, are intact. Neuroimaging visualization (fMRI) was performed while GL was gently stroked with a soft brush on her left forearm, showing that the somatosensory cortices are not activated by C-specific tactile stimulation. Conversely, the posterior insular cortex show similar activation as in healthy subjects, suggesting that the posterior insula is involved in the processing of CT-mediated touch (Olausson et al., 2002; Björnsdotter et al., 2009). Further support of the notion that posterior insula is the principal target of the CT afferents comes from a study showing preferential posterior insular activation with brush strokes performed at the CT optimal velocity of 3 cm/s, rather than at slower or faster (CT suboptimal) velocities (Morrison et al., 2011a). Interestingly, such velocity dependent activation occurs even when simply viewing others’ stroking (Morrison et al., 2011a), and it is not seen in patients with decreased C fibres density (Morrison et al., 2011b). Finally, slow brush stroking on the forearm has been seen to activate posterior insula when contrasted to slow brush stroking on the palm (Perini, et al., 2015; McGlone et al., 2012). The findings obtained with the patients suffering from sensory neuropathy (Olausson et al., 2002), as well as the somatotopical organization of posterior insular responses (Björnsdotter et al., 2009) led to the notion that the posterior insular cortex is the primary CT cortical projection area (Gordon et al., 2013; Kringelbach & Berridge, 2009; Morrison et al., 2011a). The posterior insula cortex receives information about the physiological condition of the body, such as somatosensory, nociceptive, and visceral information (Augustine, 1985), whereas it seems that the anterior part processes more complex information about emotion and self-awareness (Craig, 2011).

However, the hedonic content of affective touch cannot be processed by a single cortical region. In addition to posterior insula, other parallel or minor cortical targets to pleasant touch have been identified. As affective touch is considered a pleasant experience, it is reasonable to believe that it carries a rewarding value. Indeed, the orbitofrontal cortex (OFC), a brain region included in the reward-related circuitry (Kringelbach, 2005; O'Doherty, 2004; Schultz, Tremblay, & Hollerman, 2000), is activated during pleasant tactile stimulation (Francis et al., 1999), as well as the pregenual anterior cingulate cortex (pgACC) (Case et al., 2016). The superior temporal sulcus (STS) is another area potentially implicated in the neural processing of affective touch. Individuals with autistic traits, which present impaired abilities during tactile interactions (Robins & Dautenhahn, 2014), show reduced STS activation in response to brush stroking compared to healthy controls (Voos et al., 2013).

Despite these findings, it is still unknown how the neural processing of affective touch evolves over a prolonged period of time. The research question of **Paper III** is therefore to investigate how the brain, and specifically the neural pathway involved in short-lasting pleasant touch, responds when CT optimal touch at 3 cm/s is continuously administered for a long time (40 minutes). To the best of our knowledge, the neural processing of pleasant touch has only been examined for time scales shorter than several minutes. From the findings of paper II, it seems that CT optimal touch is perceived as pleasant for a rather long time, especially when there is velocity variation (experiment I). Following these results, in order to investigate the underlying brain activation, whole brain BOLD (blood oxygen level dependent) changes during prolonged CT optimal touch were monitored in **Paper III**. Furthermore, changes of functional connectivity (FC) during long-term stroking were explored and subjective ratings of pleasantness were collected.

1.6 The functional role of the CT afferents

Considering the assumed importance of affective touch in the domain of social interactions among individuals (McGlone, Wessberg, & Olausson, 2014; Morrison, Löken, & Olausson, 2010), and taking into account that the CT responses are optimal for tactile stimuli that are common in social interactions such as caressing and stroking (Croy et al., 2016), the “social touch hypothesis” has been conceived in order to define the functional role of the CT pathway. This hypothesis assumes that the CT afferents play a role in eliciting the subjective pleasant experience derived from gentle touch between individuals (Olausson et al., 2010; Morrison et al., 2010). Such hedonic experience is usually measured in laboratory settings through pleasantness ratings assigned to brush stroking on the hairy skin of the forearm (McGlone et al., 2012), performed at a certain velocity and force (Löken et al., 2009). Supporting the “social touch hypothesis", it seems therefore that CT-mediated touch is of importance for creating and maintaining social relationships, as for example between romantic partners (Triscoli et al., 2017) and mother-child interactions (Croy et al., 2016), and for signalling attachment and affiliative body contact with other significant ones. Moreover, slow touch at the CT optimal velocity has been shown to be particularly effective in reducing feelings of social exclusion (von Mohr et al., 2017). In these terms, it seems that CT-mediated touch is the primary channel for coding the affective, rewarding and hedonic information of a tactile stimulation (McGlone et al., 2014).

In order to further explain the functional role of the CT afferents, the "interoceptive hypothesis" has been proposed. This hypothesis emphasizes the physiological effects of affective touch on bodily processes (Olausson et al., 2010). Interoception is defined as the mechanisms involved in the perception and encoding of physiological changes in visceral body tissues (Craig, 2002). Noticeably, even if innervating the skin, the CT afferents are more physiologically and functionally related to "interoceptive" pathways (visceral innervation) rather than to "exteroceptive" ones (body surface) (Björnsdotter et al., 2010). It is thus not surprising that their principal target is the posterior insular cortex, which codes for visceral information (Kurth et al., 2010). Such "interoceptive" pathways influence the autonomic regulation of the body through the sympathetic and parasympathetic systems, which modulate heartbeat, breathing and muscles activity (Seth & Critchley, 2013). The "interoceptive hypothesis" postulates that the CT afferents play a role in the homeostatic regulation of the body by providing a balance between the sympathetic and parasympathetic systems. In these terms, homeostasis refers to the ability of maintaining a stable psychophysiological condition even under stressful circumstances (Cannon, 1932).

A further hypothesis on the functional role of the CT afferents is the so-called "thermoregulatory hypothesis". It states that CT-mediated affective touch is a phylogenetic result of thermoregulatory-related traits developed in order to promote warmth-seeking behaviours in mammals. This motivation towards social proximity in mammals likely has also the aim of creating a "safe zone" from predation exposure (Morrison et al., 2010). In the same way, CT-mediated touch among individuals such as hugging and caressing may not only have a potential role in maintaining the body temperature, but also in providing feelings of comfort and in relieving stress and anxiety (Coan et al., 2006; Vrontou et al., 2013).

1.7 The physiological effects of touch

In addition to the social, affiliative and rewarding value of touch, several studies show its beneficial effects on the well-being of the individual. Documented physiological changes are increased oxytocin levels (Light, Grewen, & Amico, 2005), decreased cortisol levels (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003), blood pressure (Weiss, 1990), and heart rate in adults (Drescher, Whitehead, Morrill-Corbin, & Cataldo, 1985; Pawling et al., 2017) as well as in children (Fairhurst, Löken, & Grossmann, 2014). Partners who use different kinds of tactile interactions, such as handholding, hugs and massages, exhibit lower blood pressure (Grewen, Anderson, Girdler, & Light, 2003), cortisol levels, and heart rate (Ditzen et al., 2007) during a social stress condition, compared to a control group with no tactile interactions involved. At a more subjective level, reduced anxiety is seen in healthy subjects (Olson & Sneed, 1995) and hospitalized patients (Heidt, 1981) after therapeutic touch sessions, and in married women who are allowed to hold their husbands´ hand during a stressing situation (Coan, Schaefer, & Davidson, 2006). As well, behavioural stress in preterm infants (e.g., gasping, grunting and moving) is reduced after 15-min-sessions of gentle human touch (Harrison, Olivet, Cunningham, Bodin, & Hicks, 1996). Finally, studies on massage therapy show that pleasant tactile stimulation increases heart rate variability (Sripongngam et al., 2015; Garnera et al., 2008). An increase in heart rate variability usually denotes a good balance between the sympathetic and parasympathetic systems, necessary for the maintenance of the overall well-being of the individual (McLachlan et al., 2010). Conversely, stressful situations lead to autonomic dysregulation involving sympathetic dominance and resulting in several stress disorders (Streeter, Gerbarg, Saper, Ciraulo, & Brown, 2012). It seems therefore reasonable to believe that gentle tactile interactions among individuals lead not only to a pleasant experience, but also to beneficial physiological effects on well-being. However, to the best of our knowledge, the speed and the pressure of the tactile stimulation were not monitored in the above studies; therefore it is not possible to ascertain that the type of touch was optimal for CT activation. Considering the proposed role of the CT afferents in the autonomic regulation of the body (i.e. the “interoceptive hypothesis”) (Olausson et al., 2010), it was of our interest to investigate the physiological effects of touch when the involvement of CT afferents was assumed to be optimized.

Following up the neuroimaging results of paper III, where a long-term paradigm was used, the aim of **Paper IV** was to determine whether long-lasting tactile stimulation performed at the CT optimal velocity (3 cm/s) had a beneficial effects on the autonomic regulation of the individuals, thus by measuring the stress response in terms of heart rate variability, salivary cortisol levels and subjective reports of stress. An eventual increase in heart rate variability and/or a decrease in salivary cortisol levels would suggest that pleasant touch prolonged for a long time has potentially positive outcomes for the homeostasis of the body, and perhaps could be used as a therapeutic tool in stress-related disorders.

2. Specific aims

Paper I: The aim of paper I was to investigate whether brush strokes manually produced or performed by a robot were comparable in terms of perceived pleasantness, as well as to determine whether the awareness of the source of the stimulation (handheld brush or led by a robot) could influence the subjective evaluation of either CT optimal or CT suboptimal touch.

Paper II: The aim of paper II was to investigate whether "satiety" for touch occurred with prolonged tactile stimulation by examining whether and how "liking" and/or "wanting" for touch changed at different stroking velocities.

Paper III: The aim of paper III was to investigate, with fMRI, whether and how the neural response changed with repeated exposure to touch performed at the CT optimized stroking velocity.

Paper IV: The aim of paper IV was to investigate whether long-lasting pleasant touch performed at the CT optimal velocity had positive effects on psychological and physiological parameters such as stress response, reward sensitivity, current mood, and interoceptive awareness.

3. Summary of Empirical Studies

3.1 Ethical approvals and funding

All the studies were performed according to the Declaration of Helsinki, and conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest. Ethical approvals for paper I, II, III and IV were granted by the Ethics Committee of Gothenburg University. Ethical approval for paper III was granted also by the Regional Medical Research Ethics Committee. All papers were supported by the Swedish Research Council Grant (grant 2011-1529). In addition, paper I was supported by a scholarship from the German Research Foundation (DFG; CR479/1-1) to IC, and paper III by a grant of the Marcus och Amalia Wallenbergs Minnesfond to IC (MAW2014.000).

3.2 Paper I

3.2.1 Participants

The participants received oral and written information prior to their participation and signed an informed consent form. They all received financial compensation for participating. Thirty-one healthy subjects (16 males) aged between 20 and 30 years (m=24.5; *sd*=2.61) were recruited locally. The majority of the participants were students.

3.2.2 Protocol and experimental design

The purposes of paper I were to determine whether brush stroking manually produced or delivered by a robotic source were evaluated equally in terms of perceived pleasantness and whether the awareness of the source of the stimulation (handheld versus robotic) influenced the subjective evaluation of pleasantness.

Four experimental conditions were randomly administered in a within-subjects design. In the first two “not-informed” conditions, the participants were not aware whether they were stroked by the experimenter or by a robot. In the subsequent two “informed” conditions, the participants were informed about the source of the tactile stimulation before each condition. The four conditions were therefore defined as “not-informed handheld stroking,” “not-informed robot stroking,” “informed handheld stroking,” and “informed robot stroking.” For the whole duration of the experiment, the participants were shielded from auditory and visual distraction by the aid of headphones delivering “pink noise” and occluding glasses whose edges prevented the participants from seeing the tactile source on their left side. The stroking in both handheld and robot conditions was performed with two identical brushes on the left dorsal forearm of the participant, either by the experimenter or by a custom-built robotic device (rotary tactile stimulator, RTS; Dancer Design, St Helen's, UK) driven by LabVIEW (National Instruments, TX)) at a calibrated force of 0.4 N. Each brush stroke was followed by ratings of pleasantness and intensity on two Visual Analogues Scales (VAS) presented on a computer screen. For all the conditions, three different brush stroking velocities were applied: "slow" (3 cm/s) (optimally activating the CT afferents), "fast" (30 cm/s), and "very slow" (0.3 cm/s) (both sub-optimally activating the CT afferents). Each velocity was repeated 3 times, with a total of 9 brush strokes per condition.

3.2.3 Questionnaires

In order to assess individual differences in tactile behaviours in communicative contexts (eg. how much we are willing to be touched, as well as how much we actually touch others in order to express ourselves), the Tactype (Deethardt & Hines, 1984) was administered. Potential symptoms of depression were assessed by using the "Beck depression inventory-II" (BDI-II; Beck & Steer, 1987). Since none of the participants presented scores within the range of moderate to severe depression, none of them were excluded from the study. The questionnaire mean scores were obtained and subsequently correlated with the ratings of pleasantness and intensity.

3.2.4 Statistical analyses

The three repetitions of each rating of pleasantness and intensity per velocity and condition were averaged. Two ANOVAs (3*2*2) for repeated measures were performed, one for pleasantness and one for intensity as dependent variables, with "velocity" (3 levels: "fast", "slow" and "very slow"), "source" (2 levels: "robot" and "handheld"), and "awareness" (2 levels: "aware" and "not aware") as within-subjects factors. Age was added as covariate and gender as between-subjects factor in the analyses. Subsequently, ANOVAs (2*2) for repeated measures were performed, separately for each of the three velocities, with "source" and "awareness" as within-subjects factors, and Bonferroni corrected at p=.017.

3.2.5 Results

A significant main effect of stroking velocity on the pleasantness ratings was found, with the CT optimized stroking velocity (3 cm/s) leading to higher perceived pleasantness than the CT non-optimized stroking velocities (30 cm/s and 0.3 cm/s). No significant differences were found between stroking at 0.3 cm/s and stroking at 30 cm/s. No significant main effects of the source of the stimulation or of the awareness of it were found on the perceived pleasantness, meaning that the brush stroking was equally pleasant when it was either handheld or performed by a robot, as well as when the participants were aware or unaware of the source of the stimulation. However, a significant interaction between awareness and velocity showed that, when stroking at 0.3 cm/s, the informed condition led to higher pleasantness ratings than the uninformed condition. Finally, no significant effects of age or gender on the pleasantness ratings were found.

For the intensity ratings, a main effect of velocity showed a linear relationship between velocity and intensity ratings, with the faster the velocity, the more intense the evaluation of the sensation. Specifically, significant differences were found between 0.3 cm/s and 3 cm/s and between 0.3 cm/s and 30 cm/s, but not between 3 cm/s and 30 cm/s. Furthermore, a main effect of source showed that, for the slower velocities of 3 cm/s and 0.3 cm/s, stroking was perceived as more intense when manually produced than when performed with the robot. No significant main effect of awareness of the source, no significant interactions, and no significant effects of age or gender on the intensity ratings were found. No significant correlations were found between the questionnaires and the pleasantness or intensity ratings.

3.2.6 Discussion

The results of paper I showed that both sources of stimulation (manually or robotically produced) provided a comparable degree of perceived pleasantness. This was true for both the CT optimized stroking velocity (3 cm/s) and the non-optimized stroking velocities (30 cm/s and 0.3 cm/s), and regardless of the awareness of the source. The similarity in the pleasantness ratings regardless of the source of the stimulation allowed assessing the convergent validity of using a robot for delivering pleasant brush strokes. This finding represented the prerequisite of paper II, III and IV, where the long-term brush stroking was delivered by a robotic source.

Supporting previous observations of the CT optimized stroking velocity being perceived as the most pleasant (Ackerley et al., 2014a; Löken et al., 2011; Löken et al., 2009; Kirsch et al., 2017), just to name few, the 3 cm/s stroking velocity was the one that achieved the highest pleasantness ratings. This was true for all four conditions: both when the stroking was manually or robotically produced, and both when the participants were aware or unaware of the source. These findings support the notion of the relationship between stroking velocity and pleasantness ratings as described by an inverted U shape (Löken et al., 2009), with the highest perceived pleasantness at the CT optimized stroking velocity.

Contrary to previous observations of the role of expectations in the evaluation of pleasant touch (Grimm, 2010; McCabe et al., 2008; Gazzola et al., 2012), the pleasantness ratings when the participants were not aware of the source of the stimulation did not differ from the pleasantness ratings when they were aware of it. It seems therefore that the attribution of the source does not change the rewarding value of pleasant touch in the present context. The contradictory results may be explained by the different degree of expectations induced in the subjects. In the study by McCabe and colleagues, two qualitatively different labels were given to the same cream (“rich moisturizing” versus “basic”), and this could have induced expectations in the subjects, leading to stronger top down regulation on the tactile experience (McCabe et al., 2008). Contrarily, in the present experiment, the subjects were not led to believe that the two brushes differed in some way, for example by saying that the robotic source was more precise than the hand in delivering the brush strokes, or that the handheld stimulation was lighter than the robot stimulation. Indeed, the similarity in the pleasantness ratings may have been due also to the identical features of the two brushes used, and this could have consequently prevented robust top down regulation. However, such paradigm allowed a strong precision and reproducibility of the results, as well as the validation of the method of using a robotic source. Noticeably, the participants were not asked about the source of the tactile stimulation; thus, despite the aid of headphones and occluding glasses, we cannot be absolutely certain that they were actually aware of it also during the "not aware" conditions. It is for future research to examine more ecological situations where the evaluation of pleasant touch may be affected by cognitive mechanisms such as expectations.

A measure of intensity was added to the experiment with the attempt of disentangle emotional components of touch (pleasantness) from physical sensations (intensity). Supporting previous observations (Löken et al., 2009), a linear relationship between intensity ratings and velocity was observed: the subjective ratings of intensity increased together with the velocity of the stroking. As the Aβ firing frequencies show a similar linear relationship with stroking velocity (Löken et al., 2009), it may be reasonable to believe that the intensity ratings reflected Aβ activation. However, evidences on the receptor level can only be provided by microneurography studies.

The handheld brush stroking was perceived as more intense than the one produced by the robot when delivered at the slower velocities (0.3 cm/s and 3 cm/s). This may have been due to tiredness, muscle fatigue, attention maintenance or distracting factors of the experimenter. All these causes may have prevented the maintenance of a constant pressure of stroking, difficult to achieve manually over a long time. Following this finding, we adapted our routine by training the experimenter to perform the brush strokes on a scale, in order to keep a constant force of 0.4 N. Results of a subsequent pilot study showed no differences in intensity ratings between different types of stimulation.

3.3 Paper II

3.3.1 Participants

Two experiments were performed. 12 healthy subjects (6 males), aged between 19 and 28 years (m=22.58; *sd*=2.78) took part in experiment I, while 17 healthy subjects (6 males), aged between 19 and 66 years (m=30.59; *sd*=11.68) took part in experiment II (one participant, 66 years old, differed substantially from the others in terms of age, but without affecting the results). All 29 participants were recruited locally. None of the participants of experiment II had taken part in experiment I.

3.3.2 Protocol and experimental design

3.3.2.1 Experiment I

The experiment adopted a within-subject design. Brush stroking stimuli were delivered on the left forearm of the participants by a custom-built robotic device (linear tactile stimulator, LTS; Dancer Design; St Helen's, UK, driven by LabVIEW software (National Instruments; Austin, TX)) (see figure 1, panel A) at a calibrated force of 0.4 N. Five brush strokes delivered back-and-forth constituted one trial, after which the participants were instructed to rate the “liking” and “wanting” of the brush stroking on two VAS presented on an iPad. The first VAS measured the concept of “liking” with the question “how pleasant was the brushing?”. The second VAS, which always appeared after the first one, measured the concept of “wanting” with the question “how much do you want another stroke of the same velocity?”. Three different brush stroking velocities were applied in a pseudo-randomized order, so that each velocity occurred no more than twice in a row: “medium” (3 cm/s) (optimally activating the CT afferents), “fast” (30 cm/s) and “slow” (0.3 cm/s) (sub-optimally activating the CT afferents). Each velocity was repeated 40 times, with a total amount of 120 trials and duration of about 50 minutes.

3.3.2.2 Experiment II

Experiment II was designed to test the development of satiety when two different velocities were applied to two different groups of subjects. The procedure of tactile stimulation was equivalent to that of experiment I, the difference being that the participants were stroked using only one velocity in a between-subjects design. Stroking velocities of 3 cm/s (optimally activating the CT afferents) and 30 cm/s (sub-optimally activating the CT afferents) were administered respectively to 8 and 9 participants. In order to maintain the same brush stroking duration as in experiment I (about 50 minutes), the 3 cm/s group received 120 trials, while the 30 cm/s group received 267 trials.

3.3.3 Questionnaires

The participants filled in three different questionnaires. The “Behavioural Inhibition and Activation Systems scale” (BIS/BAS; Carver & White; 1994) measures positive affect in response to reward through several subscales (BAS Drive, BAS Fun Seeking and BAS Reward Responsiveness), and negative affect in response to punishment (BIS). The “Temporal Experience of Pleasure Scale” (TEPS; Gard; 2006) explores individual trait dispositions in Anticipatory (reward responsiveness and imagery) and Consummatory (openness to different experiences and appreciation of positive stimuli) experiences of pleasure. Finally, the “Need for Touch Scale” (Peck & Childers; 2003) examines individual differences in preference for touch with two sub-scales: the Autotelic dimension (referring to the hedonic-oriented response towards sensory stimuli) and the Instrumental dimension (referring to aspects of pre-purchase touch that reflect outcomes directed to a purchase goal of any kind of commercially-available products). The questionnaire mean scores were obtained and subsequently correlated with the ratings of “liking” and “wanting”, with the data of experiment I and II pooled together.

3.3.4 Statistical analyses

In both experiments, the ratings for each participant were averaged, obtaining mean values for ‘‘liking” and ‘‘wanting’’ at each velocity. Linear regression analyses were performed separately with ‘‘liking” and ‘‘wanting’’ as the outcome variables and the number of repetitions as the predictor, for each velocity. In order to determine whether “liking” and “wanting” were evaluated differently depending on velocity, a multivariate analysis of variance (MANOVA) was performed with “liking” and “wanting” as dependent variables and “velocity” as the fixed factor (respectively, 0.3 cm/s, 3 cm/s and 30 cm/s in experiment I, and 3 cm/s and 30 cm/s in experiment II). Interactions’ effects were explored using post hoc t-tests corrected for multiple comparisons. Subsequently, paired sample t-tests were conducted at each velocity in order to compare the mean level of “liking” and “wanting”. In order to determine whether “liking” could significantly predict the subsequent “wanting”, a further linear regression analysis was performed for all the velocities together with ‘‘wanting’’ as the outcome variable and ‘‘liking’’ as the predictor. Finally, for stroking at 3 cm/s and 30 cm/s, independent t-tests were used to assess whether the *constant* stroking velocity of experiment II and the *mixed* stroking velocity of experiment I produced significantly different “liking” and “wanting” ratings at the end of the stroking between the two experiments.

3.3.5 Results

3.3.5.1 Experiment I

A slight but significant decrease over repetitions was found for stroking at the CT optimized stroking velocity (3 cm/s) for both “liking” and “wanting”, however they never dropped below neutral. No significant decreases were seen for the CT non-optimized stroking velocities (30 cm/s and 0.3 cm/s), whose “liking” and “wanting” ratings were stable around the neutral point for the whole duration of the brush stroking. Supporting previous observations (Ackerley, Backlund Wasling, et al., 2014; Löken et al., 2011; Löken et al., 2009), “liking” (pleasantness) was higher for the CT optimized stroking velocity than for the slower and faster velocities. The same tendency was found for “wanting.” No differences were found in neither “liking” nor “wanting” between stroking at 0.3 cm/s and 30 cm/s. Another finding showed that, while there were no significant differences between “liking” and “wanting” when stroking at 3 cm/s, “liking” was significantly higher than “wanting” when the stroking was applied with the two CT non-optimized stroking velocities. Finally, the linear regression showed that “wanting” could be positively predicted from “liking”. However, this finding must be valued carefully, due to the lack of randomization of the two VAS, where “wanting” was always subsequent to “liking.”

3.3.5.2 Experiment II

A significant decrease over repetitions was found for both the CT optimized (3 cm/s) and CT non-optimized (30 cm/s) stroking velocities, for both “liking” and “wanting.” The difference was that, for the faster velocity, the “liking” ratings ended up in the neutral range, while for the CT optimized velocity the experience at the end of the stimulation was rated slightly unpleasant. Contrarily, the “wanting” ratings decreased below the neutral point for both velocities, though faster for the 3 cm/s velocity. Another finding showed that the “liking” was higher than the “wanting” for both groups (3 cm/s and 30 cm/s). Contrary to experiment I, no significant main effect of velocity was found neither for the “liking” nor for the “wanting”. This means that the “liking” and the “wanting” ratings were similar between the two groups. Finally, for experiment I, “liking” positively predicted “wanting”.

3.3.5.3 Data of experiment I and II pooled together

The comparison between the two experiments (*mixed* versus *constant* velocity) showed that the “liking” and the “wanting” end-ratings for the CT optimized stroking velocity (3 cm/s) were significantly higher in experiment I, in which there was velocity variation, compared to experiment II, in which there was no velocity variation. No significant differences in the end-ratings of “liking” nor “wanting” were seen for stroking at the CT non-optimized stroking velocity (30 cm/s).

Finally, significant negative Pearson´s correlations were found between the mean “liking” and the BAS Fun Seeking, as well as between the BAS Fun Seeking and the mean “wanting”. Moreover, a significant positive correlation was found between the mean “liking” and the mean “wanting”. No other significant correlations were found.

3.3.6 Discussion

In experiment I, with velocity variation, the decrease in “liking” and “wanting” was exclusively observed for stroking at 3 cm/s, although CT optimal stroking was still perceived as pleasant and “wanted” at the end. It is known that 3 cm/s is the velocity most similar to a human caress (Ackerley et al., 2014a). The decrease in “liking” and “wanting” specifically for the CT optimized stroking velocity may be due to the fact that such velocity is likely the most emotionally connoted, if compared to slower or faster velocities, and corresponds to a sensory stimulus usually experienced in everyday life. In other words, it may be easier to reach satiety for known stimuli, rather than for stimuli not commonly experienced (as stroking at 0.3 cm/s or 30 cm/s). From a physiological point of view, it is worthy to consider the characteristics of the afferents involved. As CT afferents undergo fatigue after short periods of tactile stimulation (Bessou et al., 1971; Iggo, 1960; Nordin, 1990; Vallbo et al., 1999; Zotterman, 1939), the decrease in “liking” and “wanting” at 3 cm/s velocity may be related to a decrease in CT activity in response to repetitive touch. However, microneurography studies with longer periods of stimulation are required to characterize CT fatigue during 50 minutes of brush stroking. Conversely, when repeatedly stimulated, the myelinated, fast conducting Aβ fibres fatigue to a considerably less extent than the CT afferents (Barker et al., 1982), therefore Aβ fibres may have minimal or no effects on touch satiety. In this sense, the stable ratings over time for “liking” and “wanting” for stroking at the CT non-optimized velocities may have reflected Aβ activation.

CT-targeted stroking was still perceived as pleasant and wanted after 50 minutes of stroking. This may be due to the fact that in experiment I the participants experienced all velocities alternatingly. Velocity variation may have prevented the occurrence of satiety over repetitions. Hence, experiment II investigated whether satiety for pleasant touch occurred when the velocity was not varied. The results showed a similar decrease in “liking” and “wanting” for both groups

(CT optimized and CT non-optimized stroking velocities), with the “liking” ending up in the slightly negative range only for the CT optimized stroking velocity. Considering the faster decrease of “liking” and “wanting” when only one velocity was applied, it seems that tactile satiety occurs in the same way as for gustatory stimuli, where food variation prevent its occurrence (Rolls et al., 1981; Rolls & Rolls, 1997).

It is a challenge to understand whether satiety reflects more peripheral processes linked to CT fatigue or rather more cognitive mechanisms related to boredom due to the prolonged stimulation. On the one side, in experiment I the “liking” ratings for the 3 cm/s stroking velocity decreased faster than for the CT non-optimized velocities, and in experiment II they terminated in the negative range only for 3 cm/s. This indicates that satiety may be velocity dependent and therefore reflects a peripheral mechanism. On the other side, 50 minutes of protracted tactile stimulation could have led to boredom, an experience that could have altered the cognitive attentional process necessary for the evaluation of touch. The lack of boredom ratings means we cannot exclude this possibility. In fact, some subjects stated after the experiment that they had enjoyed the tactile stimulation, but found it hard to sit still for such a long time. However, if satiety were exclusively due to boredom derived from the lack of velocity variation, we would have observed an equal decrease for the two velocities in experiment II. Satiety has been defined as a phenomenon occurring when the stimulus becomes aversive (Bellisle et al., 2012), whose purpose is therefore to terminate the stimulation. Supporting this view, we may conclude that satiety for touch is both CT velocity dependent and due to the absence of velocity variation, seen that only for 3 cm/s and only in experiment II the “liking” ratings terminated in the negative/unpleasant range. On this line of inquiry, we may assume that “tactile sensory specific satiety” can occur, meaning that the perceived pleasantness for the tactile stimulus to which we have been continuously exposed is lower than for other tactile stimuli. However, this interpretation must be taken carefully since no other velocities were presented and rated in experiment II. In normal circumstances, social tactile interactions are more likely to vary in velocity and force than in a controlled experimental setting, therefore satiety to social touch may not occur so easily as in a laboratory. As well, the active seeking behaviours adopted by the individuals towards long-lasting pleasant stimulations such as massages and tactile interactions with close ones suggests that touch may have rewarding features which last for a long time.

Another interesting finding from experiment II is that, differently from experiment I and from previous observations on the higher hedonic experience of caress-like stroking at 3 cm/s compared to slower or faster velocities (Ackerley et al., 2014a; Löken et al., 2011; Löken et al., 2009), the “liking” and “wanting” ratings of the group receiving brush strokes at 3 cm/s were similar to the “liking” and “wanting” ratings of the group receiving brush strokes at 30 cm/s. The reason may be that in experiment II the participants experienced only one type of velocity, therefore they were unable to make comparisons among velocities when evaluating the “liking” or the “wanting.”

A limitation of Paper II is that it is not known whether the "wanting" question in the form that it was presented (i.e. "How much do you want another stroke of the same velocity?") really captured the concept of "wanting" as it was conceived by the authors (Berridge & Robinson, 2003). As it is believed to be triggered unconsciously (Berridge, 2009), asking for an explicit rating may not have been the optimal choice. A different measure might have been more favourable; for example, "wanting" could possibly be operationalized by letting the subjects work to obtain the reward (for example by pressing a button). Alternatively, facial electromyography (EMG) could have been useful for detecting "wanting", as it seems to be a sensitive tool for inferring affective states and emotional reactions (van Boxtel, 2010; Dimberg, 1990). This observation further validates the requirement of the "wanting" measure. A further limitation is that "wanting" was always preceded by "liking." Consequently, the causal relationship between the two concepts can be a result of this method. Future studies adopting this paradigm should randomize the order of appearance of "liking" and "wanting" in order to have more trustful results.

3.4 Paper III

3.4.1 Participants

Twenty-five healthy subjects (10 males), right-handed, with normal or corrected-to-normal vision by contact lenses, aged between 19 and 38 years (m=23; *sd*=3.85) were recruited locally. The majority of the participants were students.

3.4.2 Protocol and experimental design

Images were acquired with a 3-Tesla MRI scanner equipped with a 32 channel head coil. Thirty-seven volumes were obtained during each block (666 volumes in total) in 40 transverse ascending slices. The participants lay in the scanner and were scanned during 18 blocks of two minutes duration each. The first and the last block constituted resting state baselines, while the 16 blocks in-between represented the active tactile stimulation condition. During this condition, the participants were brush stroked on their left forearm, continuously back and forth for about 40 minutes, with a custom-built MR-compatible robotic device (linear tactile stimulator, LTS; Dancer Design; St Helen's, UK, driven by LabVIEW software (National Instruments; Austin, TX)) (see figure 1, panel A) at a replicable force of 0.4 N and a stroking velocity of 3 cm/s, i.e. the optimal speed to elicit CT afferents discharge and typically experienced as the most pleasant (Ackerley et al., 2014; Löken et al., 2009). After every 2 minutes, the participants were instructed to rate the perceived pleasantness of stroking on a VAS presented on a computer screen positioned in front of them, which they could see via a mirror on the head coil.

3.4.3 Questionnaires

The participants filled in the same questionnaires as for paper II, i.e. The "Behavioural Inhibition and Activation Systems scale" (BIS/BAS; Carver & White; 1994), the "Temporal Experience of

Pleasure Scale” (TEPS; Gard; 2006), and the “Need for Touch Scale” (Peck & Childers; 2003). Moreover, the “Subjective Measure of Positive Affect and Negative Affect Scale” (PANAS; Watson et al., 1988), in which high positive affect reflects high energy, full concentration, and pleasurable engagement, whereas high negative affect reflects subjective distress and unpleasurable engagement, was administered. The questionnaire mean scores were obtained and subsequently correlated with the pleasantness ratings.

3.4.4 Statistical analyses

3.4.4.1 Touch ratings

In order to determine how the perceived pleasantness of stroking evolved over time, a linear regression analysis was performed with the pleasantness ratings per block as outcome and the number of blocks as predictor. Two one-sample t-tests were performed on block 1 and block 16 in order to evaluate whether touch was perceived as significantly pleasant at the beginning and at the end of the experiment. Furthermore, a paired samples t-test between block 1 and block 16 was run in order to examine whether the ratings differed at the beginning compared to the end of the experiment. Finally, a paired samples t-test was used to compare the *sd* of the single ratings in blocks 1-8 with the *sd* of the single ratings in blocks 9-16.

3.4.4.2 fMRI data

Data were pre-processed with motion correction. Potential scanner drift was corrected by adding the global mean as covariate in the analyses. Firstly, a whole-group comparison between the first and the last baseline was performed. As no significant differences were found, for the subsequent first level analyses 16 contrast files per subject were obtained by comparing the 16 stroking blocks to the first baseline. Moreover, 6 directions of movement parameters were included as regressors. Secondly, in order to explore the overall effect of stroking, a full factorial second level analysis was performed with the 16 contrast files per subject (stroking blocks) as within-subjects factor. Thirdly, t-tests were used for comparing the activations in the first and last block to each other. Finally, in order to investigate the relationship between neural reward activation and perceived pleasantness, the pleasantness ratings were added as covariates in the full factorial second level analysis. As the ratings follow different patterns in the first and second half of the experiment, the analysis was performed separately for the first 8 blocks and the last 8 blocks.

3.4.4.3 Functional connectivity

Networks of functional connectivity were explored for the posterior insula. Specifically, voxel-seed correlations estimated through temporal correlation maps were performed over each block between an insular seed, previously created, and the rest of the brain. A subsequent full factorial analysis with the within-subjects factor block (16 levels) was computed. Coupling of the posterior insular seed was consequently assessed in the first and in the last stroking block, separately. Furthermore, t-contrasts between the first and the last stroking block, masked inclusively by activation obtained in the first block, and t-contrasts between the last and the first stroking block, masked inclusively by activation obtained in the last block, were performed.

3.4.5 Results

3.4.5.1 Touch ratings

The tactile stimulation remained pleasant throughout the experiment. In fact, if at the beginning the ratings were in the positive range and they never dropped below neutral. Accordingly, the pleasantness ratings for the first block were significantly higher than those for the last block. A steady decrease was observed during the first half of the experiment (blocks 1-8), while the ratings plateaued during the second half of the experiment (blocks 9-16). A positive correlation was seen between the pleasantness ratings and the TEPS Consummatory Scale, meaning that the people who were more inclined to experience rewarding feelings liked the stroking more.

3.4.5.2 fMRI data

Strong responses to touch versus baseline in the whole brain were seen in wide activation clusters: cluster one encompassed subdivisions of the contralateral (right) primary and secondary somatosensory cortices (SI and SII), posterior insula, right inferior frontal gyrus, caudate, putamen and OFC, bilaterally. Cluster two expanded to the ipsilateral (left) SII, SI and posterior insula. Cluster three included the left inferior, middle and superior temporal gyrus.

The development of response to pleasant touch over time was examined through the comparison between the first and last block. Activation in right middle and superior occipital cortex, as well as bilaterally in SII (subdivision OP1) decreased over time. At the same time, activation in right OFC, putamen, SII (subdivision OP3) and middle temporal gyrus increased for the first half of tactile stimulation (about 20 minutes) and plateaued afterwards.

With an exploratory aim, the pleasantness ratings were added as covariate in the analysis. The results showed that in the first half of the experiment the ratings were positively correlated to activation in SI and middle frontal cortex. Contrarily, in the second half of the experiment they were positively correlated to SI, orbitofrontal regions, putamen, and superior temporal gyrus.

3.4.5.3 Functional connectivity

At the beginning of the experiment, FC was seen between posterior insula and anterior cingulate cortex, amygdala and hippocampal and parahippocampal regions. At the end of the experiment, posterior insula was coupled to the middle cingulate region and to striatal areas such as putamen and caudate, particularly pronounced in the last block. Throughout the whole experiment, posterior insula was connected bilaterally with somatosensory areas.

3.4.6 Discussion

Replicating the results of paper II, a decrease in pleasantness during prolonged brush stroking was seen also in paper III, although the stimulation never became unpleasant not even after 40 minutes of stroking. As well, corroborating previous findings (Olausson et al., 2002; Olausson et al., 2008, Lamm et al., 2015; Rolls et al., 2003; Francis et al., 1999; Perini et al., 2015; Morrison et al., 2011a), the overall neural response to pleasant touch was observed in the primary and secondary somatosensory cortices (SI and SII), areas included in tactile sensory processing, in posterior insula, i.e. the major CT-targeted area, as well as OFC, a region widely known to be part of the reward system. In line with another study (Perini et al., 2015), we found activation also in caudate and putamen. Such striatal activation may be explained by the longer duration of the stimulation adopted in our experiment compared to previous studies.

During the prolonged stimulation, a decrease in the somatosensory cortices was seen, likely reflecting peripheral habituation of Aβ fibres, whose activation is known to be encoded in SI and SII (Chapman, 1994; Ploner et al., 2000; Schaefer et al. 2006). This finding is supported by the initial decrease and subsequent plateau of the perceived pleasantness, which may be due to reduced perception of the stimulus over time. On the other hand, an initial increased activation and subsequent stabilization was observed for OFC and putamen. It may be reasonable to think that the high activation in somatosensory cortices at the beginning of the stimulation promoted the processing of the discriminative features of touch, which were experienced as novelties, while the high activation in reward-related networks at the end of the stimulation reflected the processing of the affective features of touch. This interpretation is also supported by the significant correlation between pleasantness ratings and OFC during the second half of the experiment, a result previously observed also with a shorter period of pleasant tactile stimulation (Rolls & Grabenhorst, 2008). As well, both at the beginning and the end of the stroking, activation in the major CT-targeted region posterior insula was coupled to somatosensory activation in SI and SII, while only at the end FC was seen between posterior insula and striatal activation in putamen and caudate. It may be possible that posterior insular activity served for recruiting reward-related areas, a neural mechanism likely involved in the hedonic experience during tactile interactions and social bonds among individuals.

A noteworthy finding of paper III concerns the opposite pattern observed in explicit pleasantness ratings, which decreased over time, and implicit neural activation of OFC and putamen, which increased instead. As OFC is part of the reward network (O'Doherty, 2004), it would have been more intuitive to observe reduced activation, concomitant with the decreased pleasant experience. However, despite the decrease in ratings, the experience was still experienced as slightly pleasant at the end of the stroking. As well, besides encoding for rewards (Kringelbach, 2005), another role of OFC is to monitor updates in reward preferences over time (Ostlund & Balleine, 2007), for example when a previously rewarding stimulus is no longer rewarding, and a previously non-rewarding stimulus suddenly becomes rewarding (O'Doherty et al., 2003). Hence, in our study the increased activation of OFC during the first half of the experiment might have tracked the change (decrease) in the rewarding value of stroking, reflected in the ratings. The relationship between OFC activation and perceived pleasantness observed only during the second half of the experiment may be due to the fact that at the beginning of the stroking, not only pleasantness but also other aspects of the stimulation were encoded, such as novelty and intensity. Conversely, after 20 minutes, when the stimulation was not new anymore, the ratings reflected pleasantness more trustingly (and indeed they plateaued). Hence, the significant relation with OFC emerged. In these terms, a limitation of paper III is the lack of intensity or novelty ratings, which might have allowed capturing more in depth the changes in the subjective experience. If it is reasonable to think that, initially, not only pleasantness but also other qualities of the stimulation were processed, then a higher perceived intensity or sense of novelty would have been observed at the beginning of the stroking. Afterwards, when the stimulation was no longer experienced as new, these ratings would have expected to decrease. Hence, such information would have been of importance for corroborating the role of OFC in updating the reward aspect (i.e. pleasantness) of stroking during the second half of the experiment.

Finally, another limitation of paper III is the lack of a concomitant CT non-optimized condition. Without such control, we cannot assume that the observed neural mechanisms are exclusive to CT optimal touch. However, the observed activation of the major CT-targeted region posterior insula, and its role in coupling both somatosensory and reward areas during the whole duration of stroking, suggests that CT-signalling was important for obtaining these neural effects.

3.5 Paper IV

3.5.1 Participants

Forty healthy subjects (18 males), aged between 18 and 51 years (m=27.58; *sd*=8.38) were recruited locally. The first 20 participants (9 males), aged between 20 and 39 years (m=25.7; *sd*=5.42) were assigned to the experimental “brush stroking” condition, while the next 20 participants (9 males), aged between 18 and 51 (m=29.45; *sd*=10.35) were assigned to the control “vibration” condition.

3.5.2 Protocol and experimental design

Based on the observed changes in brain activation during long-lasting touch at CT optimized stroking velocity in paper III, the following study aimed to determine whether these effects at the neural level had also physiological correlates. Hence, in paper IV several psychological and physiological variables were tested before, during, and after prolonged CT optimal (3 cm/s) brush stroking: stress response, reward sensitivity, mood and interoceptive awareness. Interoceptive awareness is defined as the ability to perceive visceral signals (Pollatos et al., 2007) or, in other terms, the perception of the physiological condition of the body (Schandry, 1981; Tsakiris, Tajadura-Jimenez, & Costantini, 2011). Stress response was operationalized as heart rate variability (HRV) (autonomic stress response), salivary cortisol levels (endocrine stress response) and self-reported stress (subjective stress response). Mood and reward sensitivity were operationalized as self-reported mood and responsiveness to pleasant odours. Finally, interoceptive awareness (also called "visceroception" or "autonomic awareness, i.e. the ability of perceiving bodily processes) was measured with the heart beat perception test (Schandry, 1981), which detects the accuracy of detection of one's own heart beat (Schandry, 1981; Pollatos et al., 2007; Wölk et al., 2014). As well, in order to control for potential alterations of tactile sensitivity, the von Frey monofilament test was performed with a staircase routine (Jönsson et al., 2015). Heart rate was monitored during the actual tactile stimulation (for subsequent HRV analyses) and during two resting intervals of 5 minutes each, before and after the stimulation. All the other variables were only measured before and after brush stroking.

In order to rule out potential unspecific test effects, a control condition with vibration was employed for the second half of the sample (between subjects design). Vibration was chosen because it is known to activate CT afferents to a lesser extent than brush stroking (Bessou et al., 1971; Wiklund Fernström et al., 2002). The procedure of tactile stimulation for the experimental group was equivalent to that of paper III. The participants were stroked continuously back and forth for about 35 minutes with a custom-built robotic device (linear tactile stimulator, LTS; Dancer Design; St Helen's, UK, driven by LabVIEW software (National Instruments; Austin, TX)) (see figure 1, panel A) at a replicable force of 0.4 N and a stroking velocity of 3 cm/s. For the control group, vibration was applied through a custom-built piezoelectric element at a predefined force of 0.4 N +/- 0.05, and a constant frequency of 100 Hz (see figure 1, panel B), continuously and without interruption for an equal duration (about 35 minutes). For both groups, pleasantness (and intensity) ratings were collected after every two minutes for a total amount of 16 ratings, through two VAS presented on a computer screen.

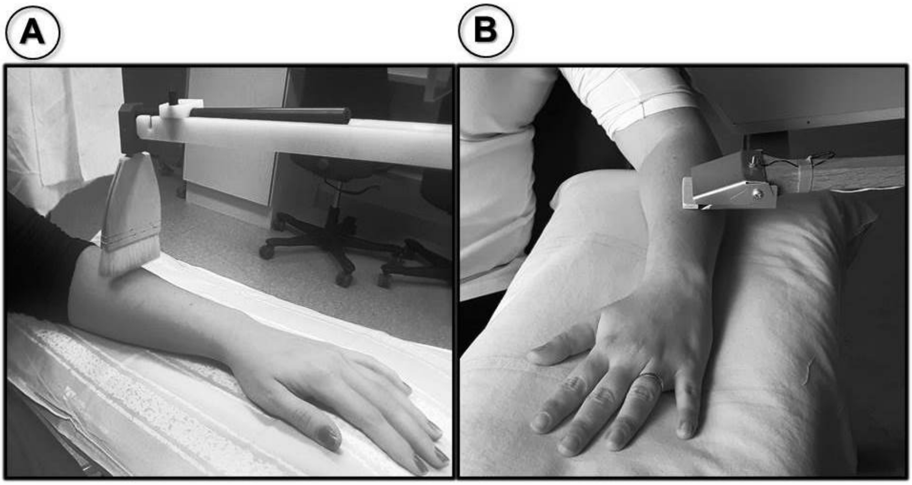

Figure 1: Linear tactile stimulator (LTS) for high-precision brush stroking used in papers II and III (panel A), and piezoelectric element for vibration used in paper IV (panel B).

3.5.3 Questionnaires

Two questionnaires evaluating the degree of reward sensitivity and current mood were administered to the participants before and after the experiment. The “Snaith-Hamilton Pleasure Scale” (Snaith et al., 1995) measures hedonic tone, or ability to experience pleasure. The “Multidimensional Mood State Questionnaire” (MDMQ; Steyer, Schwenkmezger, Notz, & Eid, 1997) evaluates the current mood through three different scales: “Good – Bad”, “Calm – Nervous” and “Awake – Tired”. Subjective stress response was assessed before and after the experiment with the “Arnetz & Hasson Stress Questionnaire” (Andersson, Johnsson, Berglund, & Öjehagen, 2009). For each questionnaire, two mean values were obtained respectively for the pre- and post-test; the differences post- versus pre-test were computed and subsequently correlated with the other dependent variables.

3.5.4 Statistical analyses

Salivary cortisol was collected 4 times. The total hormone concentrations and the cortisol response to the stimulation were subsequently obtained. HRV was calculated for each of the 16 blocks during tactile stimulation and for the two resting intervals. HRV was operationalized in the time-domain parameter SDNN (standard deviation of normal to normal inter-beat intervals), which is a measure of high- and low-frequency oscillations in inter-beat intervals, reflective of perturbations in the autonomic tone (Pope et al., 1999).

The heart beat perception test was performed before and after the experiment. The participants were asked to quietly count their own heart beats for three time intervals, and subsequently to report the counted number. During the task, the actual heart rate was monitored. Two cardioceptive accuracy indices, pre- and post-test, were obtained with the formula used in a previous study (Wölk et al., 2014). During the odours evaluation test, three different odours were presented (6 trials in total) and the participants rated the pleasantness and intensity. Two mean pleasantness ratings and two mean intensity ratings, pre- and post-test, were calculated. Finally, the von Frey monofilament test was performed on the left dorsal forearm. Four reversal points were averaged separately for the pre-test and post-test.

For all dependent variables, the difference in the mean values between the post-test and the pre-test was computed in order to obtain a differential value pre- versus post-test Subsequently, Bonferroni´s corrected correlations were computed separately for the two groups (brush stroking and vibration) among these differential values. In order to determine whether there was a stimulation dependent change *over time*, significant group differences and/or interactions, pleasantness and intensity ratings as well as cortisol levels and HRV were separately submitted to a linear mixed model analysis (LMM). For all LMMs, “subjects” and “age” were added as random combinations in order to control for random effects among subjects, and “tactile stimulation” (“brush stroking” and “vibration”) was used as one of the fixed factors. The other fixed factors were: “block number” (16 levels i.e. blocks) for pleasantness and intensity ratings, “collection time” (4 time-points) and “time of the day” (“morning” and “afternoon”) for cortisol levels, and “block number” (18 levels i.e. 2 baselines and 16 blocks) for HRV. As HRV differed between groups (see results), pleasantness and intensity were added as further fixed factors in order to determine whether such difference was due to the higher perceived pleasantness and/or intensity of brush stroking compared to vibration.

In order to determine whether there was a stimulation dependent change *before versus after*, significant group differences and/or interactions, the odour pleasantness and intensity ratings, the mean questionnaires scores, the cardioceptive accuracy indices and the skin sensitivity values were separately submitted to a LMM analysis. “Tactile stimulation” (“brush stroking” versus “vibration”) and “session” (“before” versus “after”) were used as the fixed factors, and “subjects” and “age” as random combinations.

3.5.5 Results

A main effect of tactile stimulation on the pleasantness ratings was found, meaning that the brush stroking was experienced as more pleasant than vibration. As well, a decrease in the pleasantness ratings over time was observed for both groups, ending in the slightly negative range. For the brush stroking group, the ratings were above the neutral point until about 20 minutes from the onset of the stimulation (until ~ block 9), and afterwards they dropped below the neutral point. At the same time, brush stroking was rated as more intense than vibration, while it was stable over time for both groups.

Salivary cortisol levels did not differ between brush stroking and vibration and they decreased over time for both groups. As well, they were higher in the morning than they were in the afternoon. The HRV (SDNN) significantly increased over time only for brush stroking, and this was due to both its higher pleasantness and its higher intensity compared to vibration. Specifically, the SDNN showed an initial increase until about 20 minutes from the onset of brush stroking (until ~ block 9), and it plateaued afterwards. Conversely, it remained stable for vibration.

No other significant main effects or interactions were found for the other dependent variables (tactile sensitivity, interoceptive awareness, reward sensitivity, and mood).

The “pleasure scale change” of the “Snaith-Hamilton Pleasure Scale” (representing reward sensitivity and mood) showed a significant negative correlation with the “tactile pleasantness change” for the brush stroking group only. Thus, the less the perceived pleasantness for brush stroking decreased over time, the higher the score of the pleasure scale after the tactile stimulation was, if compared to the one before. No further significant correlations were found.

3.5.6 Discussion

Paper IV demonstrated that prolonged CT-optimal touch has beneficial effects on the autonomic system. The stress index HRV, operationalized through SDNN, at the onset of the tactile stimulation was stable and similar for both the experimental brush stroking and the control vibration groups. However, after ~ 13 minutes from the onset and until the end of the experiment, it increased only for brush stroking. Significantly related to the HRV increase, and replicating the findings of a previous study (Davidovic et al., 2016), CT-targeted stroking touch was also perceived as more pleasant (and more intense) than vibration. Autonomic well-being is usually reflected by an increment in SDNN (McLachlan et al., 2010). This means that long-lasting pleasant touch performed at CT optimized velocity might have beneficial physiological effects on the overall healthy state of the individuals. In these terms, it has been proposed that affective touch plays a role as a physiological regulator, or stress buffer, against potentially disadvantageous and maladaptive responses (Morrison, 2016). As well, Pawling and colleagues showed that CT-targeted touch was not only the most pleasant, but it also produced greater heart rate deceleration than non-CT targeted touch (Pawling et al., 2017), likely reflecting relaxation. A limitation of paper IV concerns the fact that vibration possibly activates CT afferents as well, although to a lesser extent compared to brush stroking (Bessou et al., 1971). However, vibration was chosen as control condition because it seems to be the best alternative among others, such as static touch or brush stroking at CT-suboptimal velocities, which likely activate CT afferents to a greater extent than vibration (Vallbo et al., 1999).

Differently from the exclusive effect of CT-targeted touch on HRV, salivary cortisol levels decreased irrespectively of the group. This likely means that the endocrine and autonomic systems are differently responsive to sensory stimuli and that SDNN is more sensitive to affective touch. The unspecific effects on salivary cortisol may have two different explanations. On one hand, cortisol levels may have declined with the simple passage of time, due to the relaxed position of the subjects who were comfortably lying on a hospital bed for about 35 minutes. On the other hand, the decrease in cortisol levels may be an unspecific effect of any kind of tactile stimulation: indeed, a similar decrease has been shown while being tactually stimulated by a huggable human-shaped device (Sumioka et al., 2013) and after a single session of Swedish massage (Rapaport et al., 2010). In these terms, a limitation of paper IV regards the absence of a control condition without touch (as vibration involves touch). For example, a potential similar decrease in cortisol levels observed during a resting condition may have allowed explaining the cortisol reduction as a consequence of the simple passage of time. Conversely, the absence of a potential similar decline during rest would have led to conclude that a decrease in cortisol occurs only with (any kind of) tactile stimulation.

Finally, no effects of brush stroking compared to vibration, as well as no effects of session (after tactile stimulation compared to before) were observed for any of the other dependent variables, i.e. tactile sensitivity, interoceptive awareness, reward sensitivity and mood, and neither for the subjective stress response. The lack of relation between CT-targeted touch and interoceptive awareness has already been observed (Crucianelli et al., 2017). Overall, while no alterations in the above domains were observed, the effects of prolonged pleasant touch at the CT optimal velocity seem to target exclusively the autonomic nervous system regulation.

4. General discussion

Paper I showed that CT optimized (and CT non-optimized) stroking led to similar pleasant experiences regardless the source of the stimulation (manually or robotically produced). The positive findings allow the application of either one or the other source of stimulation depending on which is more optimal in that particular experimental or clinical setting. On one hand, handheld tactile stimulation could be applied in situations where a robotic source is not available or applicable, such as with certain clinical populations or small body parts. On the other hand, robotic tactile stimulation could be used in paradigms whit prolonged tactile stimulation, allowing a higher degree of reproducibility than the one achieved manually. Moreover, such similarity in the pleasant experiences between handheld and robotic brush stroking allowed determination of the convergent validity of the two measures, and the consequent application of a robotic source for delivering brush strokes in long term paradigms such as the ones used in paper II, III and IV. As well, the comparable degree of pleasantness between the “aware” and “not aware” conditions leads to the conclusion that CT optimal touch is not much affected by top down mechanisms in the present context.

From **Paper II** we can conclude that satiety to pleasant touch takes a very long time to occur. The finding that the caress-like stroking never becomes unpleasant not even after 50 minutes leads to the interpretation that a rather longer time is required before that CT optimal touch is perceived as aversive. This view supports the studies investigating the hedonic effects of touch massage protracted for longer than 50 minutes (Lindgren et al., 2014; Lindgren et al., 2010). Therefore, also during social interactions, a human caress is likely to maintain its rewarding value even when protracted for a long time. If considering that in ordinary circumstances, caress-like interactions are likely to vary for example in type and direction of the strokes, we may conclude that satiety for touch in everyday life may take even longer to occur than in a laboratory setting. It is, however, unknown whether the pattern would be similar for touch by a human hand. While being more ecologically valid, the use of a human hand, can lead to several confounds in the perception and evaluation of the pleasant experience, such as cold or sweaty hands, like or dislike towards the toucher, etc. As well, in situations when interpersonal touch occurs, different cognitive factors such as the current mood or the relationship with the touch giver may play a role. Therefore satiety to touch is likely affected also by such central mechanisms.

To the best of our knowledge, there has never been an attempt to investigate brain activation during prolonged touch. The findings of **Paper III** showed that long-lasting touch not only has hedonic conscious effects which last for time scales longer than several minutes (replicating the findings of paper II), but also that, alongside somatosensory areas, it activates brain regions involved in the reward system, such as OFC and striatal regions. Such findings might help explaining why prolonged pleasant touch, such as caressing and stroking, often happens between intimate partners and family members, signalling deep emotion and affection. In other words, the long duration of experienced pleasantness and the underlying neural mechanisms suggest that long-lasting stroking has rewarding effects in humans which are robust against satiety. Overall, it seems that the ongoing pleasant experience during long-lasting touch and the concomitant role of OFC in reward updating may be of importance for maintaining long-lasting social tactile interactions.

The results of **Paper IV** demonstrated that prolonged CT optimal touch improves the autonomic stress response, as shown by the increased activity of the parasympathetic system. It seems therefore that the hedonic conscious experience deriving from stroking at the CT optimized velocity has a physiological correlate reflected by positive changes in HRV. If such beneficial autonomic effects were seen in an artificial lab situation, where pleasant touch was performed with a brush stroking by a robotic device, then in real life situations, where pleasant touch occurs in the form of caresses among individuals, its effects on the stress response may be even greater. This can be reasonable to conclude because a caress carries a deeper emotional and affective value than a brush stroke. Future research could examine the effects of touch in more ecological situations, for example by using a human hand for delivering the stroking.

Interestingly, SDNN in paper IV increased during prolonged brush stroking with a very similar trend as OFC activation in paper III: they both increased at the beginning of the brush stroking plateaued after about 20 minutes. Thus, knowing the role of OFC in reward encoding (Francis et al., 1999), it may be that CT-targeted touch leads to positive effects at both the neural and autonomic level. Supporting this view, an association between OFC activation and cardiovascular autonomic activity has been found in response to affective stimuli (Cechetto, 2014; Lane, 2001). As well, OFC has been shown to have direct monosynaptic projections to brainstem autonomic centres (see Berntson et al. 1998). Hence, OFC may serve as a modulator of the heart rate activity, and more specifically of the parasympathetic tone (Ter Horst & Postema, 1997). Beside the possible relation between OFC activation and autonomic response, it is interesting to note that such implicit physiological effects do not have a straightforward explicit correlate because the pleasantness ratings decreased over time in both studies (and noticeably, similarly to the “liking” ratings for the CT optimal velocity in paper II). In paper IV, the stroking experience became slightly unpleasant at the end, likely reflecting a reduction of the affective value of touch over continuous stimulation. As for OFC activation in paper III, it would have been more intuitive to observe a decrease in HRV concomitant with the reduced pleasant experience. However, this opposite trend may be due to a second, less intuitive, role of HRV. Besides reflecting physiological well-being, HRV has been proposed to be an indicator of safety (Thayer, 2012). Presumably, at the beginning of the experiment, the stroking might have been perceived as a pleasant novelty, which ceased to be so and started to be experienced as a safe, neutral routine only after some time. Hence, the increase in HRV and the concomitant decrease in the pleasantness ratings were observed. Supporting this view, the increase in HRV observed during brush stroking, but not during vibration, was significantly related to its perceived pleasantness (and intensity). However, this interpretation is speculative, since the participants were not asked to evaluate how much the stimulation was experienced as a novelty or a safe routine.

To provide a possible explanation to the decrease in cortisol levels, it may be that this endocrine response is related to the change in neural response observed in paper III. Specifically, the increased activation in reward-related areas during prolonged touch at the CT optimal velocity may have an endocrine correlate expressed in the decreased cortisol levels, meaning that pleasant touch has a beneficial effect on both the neural and endocrine systems. Supporting this view, greater neural activity in OFC was observed in association with lower diurnal cortisol levels in healthy subjects (Putnam et al., 2008).

In summary, the present thesis demonstrated that CT optimal touch is a pleasurable experience regardless of whether the brush stroking is manually or robotically performed, and confirmed previous findings regarding the CT optimal velocity (3 cm/s) as being perceived as the most pleasant one. Moreover and importantly, the awareness of being stroked by either the robot or the experimenter did not affect the degree of perceived pleasantness in the present context, meaning that pleasant touch in this particular laboratory setting was robust against this kind of potential top down modulation. As well, when prolonged for time scales longer than several minutes, CT optimal touch has both conscious and physiological effects. Corroborating the “social touch hypothesis” on the functional role of the CT afferents in eliciting the subjective pleasant experience derived from gentle touch (Olausson et al., 2010; Morrison et al., 2010), we have demonstrated that touch performed at the CT optimized stroking velocity is a pleasant experience even when prolonged for a rather long time. This finding was the main focus of paper II and it has been further replicated in paper III and IV, where the CT stimulation never became particularly unpleasant, not even at the end of the experiments. In other words, we have observed that pleasant touch is robust against satiety, especially when the individuals experienced more than one stroking velocity alternatingly. Besides the subjective reports of pleasantness, a further support to the notion that CT optimal touch is an emotional experience comes from the observation that the repeated touching activates specific brain regions involved in the reward-related network, such as OFC and parts of the striatum (Kringelbach, 2005).

The present findings suggest that satiety for touch is subtle if compared to satiety for the chemical senses such as taste and smell. Indeed, in the case of gustatory and olfactory satiety, a certain food is not liked and desired anymore (thus becomes aversive) after repeated consumption (Bellisle et al., 2012; Havermans et al., 2009; Nasser, 2001). As well, the pleasure attributed to specific odours alternatingly presented (“liking”) and the willingness of smelling them again (“wanting”) steeply decrease in male participants after only few exposures (Triscoli et al., 2014). The reason why the rewarding value of touch lasts for a long time may be due to the fact that, in everyday life, tactile interactions are affected by different contextual aspects. For example, when individuals are caressed or cuddled for a rather long time, they enjoy not only the physical contact *per se*, but they also obtain a certain degree of pleasure from the situation, most likely calm and intimate, from the person providing the tactile stimulation, and/or from a more general feeling of warmth and reassurance. It may be therefore a broader set of factors that allow the rewarding experience of touch. Also, being in a laboratory setting, despite being stroked with a brush by an experimenter or a robotic device, may not closely resemble (or may not have the same ecological value of) the tactile interactions usually experienced in everyday life. It still assumes a certain degree of comfort and relaxation, i.e. it provides a harmless situation which is unlikely to become aversive. Conversely, for stimuli such as food, satiety may be stronger because it has a survival function: it acts as a warning signal that the intake is becoming “too much” and is dangerous for the health of the individual.

The effects of affective touch are not limited to its hedonic perception at both a conscious and neural level. The present findings also provided concrete evidence in support of the “interoceptive hypothesis,” which proposes a role of the CT afferents in providing a balance between the sympathetic and parasympathetic systems (homeostatic regulation) (Olausson et al., 2010). Specifically, the present work showed that touch also has positive physiological consequences on bodily processes, as documented by an increase in HRV during repeated tactile stimulation at the CT optimized stroking velocity. Besides the potential role of the CT afferents in inducing these effects (inferable from the fact that the velocity of the stroking was CT optimized), two further important pieces of evidence were raised from the current study. Firstly, these beneficial autonomic effects occurred already after few minutes of exposure to touch and lasted for a rather long time, and secondly, they occurred in absence of previously induced stressors, commonly used in previous studies on the role of social tactile interactions on physiological changes (Drescher et al., 1985; Ditzen et al., 2007; Grewen et al., 2003; Olson & Sneed, 1995). This may mean that the individuals can physiologically benefit from being continuously caressed and stroked even when they are in a “neutral” (not stressful) state, and that these effects are quickly effective. In fact, touch promotes well-being not only by reducing stress, but also independently of it (Jakubiak & Feeney, 2017). In conclusion, it seems that pleasant touch optimally activating the CT afferents has a substantial rewarding value, which persists for a rather long time. Considering these findings, it is therefore easy to understand the fundamental role of affective touch in promoting affiliative behaviour and attachment between individuals, and, ultimately, in representing the foundation of all relationships.

4.1 Limitations and strengths

It may be noteworthy to discuss the debate concerning difficulties with some estimation tools, such as the use of VAS subsequently analysed with parametric statistics. Some authors claim the non-linear nature of the VAS, which should be analysed with non-parametric statistics for ordinal data (Kersten et al., 2012). They warn about the misuse of VAS, treated as interval scales and therefore analysed parametrically, which leads to erroneous results. The assumption of these authors is that VAS have instead an ordinal nature. Due to this, change scores cannot be used to compare changes among individuals, as a given change in one subject may be of different magnitude than the same apparent change in another subject, and that VAS change scores may over- or underestimate changes resulting from the experimental condition (Kersten et al., 2012). Likewise, despite the fact VAS are sometimes preferred because they provide a finer distinction in the response options compared to numerical rating scales, some patients find it difficult to rate their pain intensity on a VAS (Kersten et al., 2012). Other authors disagree with the above assumptions. Price and colleagues claim instead that parametric statistics are entirely appropriate for VAS (Price et al., 2012). According to them, VAS fulfil several criteria validating their ratio and interval properties, such as the presence of a zero point (Price et al., 1983), high test-retest reliability and repeatability (Rosier et al., 2002), and also simplicity and ease of use (Jamison et al., 2002). They thus conclude that the assumption that the VAS lack psychometric features is not supported by evidence (Price et al., 2012). Beyond the debate, it must be noted that Kersten and colleagues questioned the use of VAS exclusively for measuring pain intensity in patients undergoing rehabilitation programs; therefore, it may be that VAS are less suitable for clinical contexts compared to experimental situations where hedonic ratings are collected in healthy participants. Likewise, VAS for measuring pleasantness to touch have been already extensively used in previous related studies (Ackerley et al., 2014a; Etzi & Gallace, 2016; May et al., 2014; Keizer et al., 2017; Olausson et al., 2002; Luong et al. 2017; Ebisch et al., 2014), just to name few. Therefore, we can conclude that VAS measurements in the present field are “common practice.” With that being said, and given the assertions of Prince and colleagues, we believe that the use of VAS for measuring pleasantness and intensity in the current thesis was the most appropriate option, which provides more intervals and allows responding with greater precision compared to numerical rating scales (Funke & Reips, 2012).

Another limitation of the data is that they are restricted to a specific sample, such as from western, educated, industrialized, rich, and democratic (WEIRD) Countries, who are assumed to be the least representative populations for generalization, when addressing questions about the human nature (Henrich et al., 2010). Consequently, it may be that individual or cultural characteristics, belonging to the specific group involved, modulated the results. In these terms, the arising question is whether and in what degree affective touch is universal rather than culturally specific. Cross-cultural studies on tactile interactions have shown some differences among ethnic groups. For example, in a study exploring touch in cafes, couples of San Juan, Puerto Rico, touched each other on average a hundred times per hour, while those in London averaged zero touches per hour (Jourard, 1966). For what concerns the current work, we have seen that prolonged touch is perceived as a positive experience (and has beneficial physiological effects) for a rather long time. We can therefore hypothesise that touch satiety could take even longer to occur for those cultures classified as “high-contact countries”, such as Southern Europe and Latin America, where people touch each other often (McDaniel & Andersen, 1998), compared to the so-called “low-contact countries”, such as Northern Europe, USA or Japan (McDaniel &

Andersen, 1998), i.e. the category where most likely the samples used in these papers were included. Also individual (rather than cultural) factors may play a role in shaping the occurrence of touch satiety; for example, people with low self-reported touch exposure rated short-lasting touch as less pleasant than the controls, especially when touch was performed at the caress-like (3 cm/s) velocity (Sailer & Ackerley, 2017). Nevertheless, it could be that for these "low-contact" groups, long-lasting touch may have a strong beneficial effect at the physiological level, because they may actually be more "in need." This could mean that, when they are exposed to long-lasting touch, they profit to a higher extent than people who experience touch more often.

A related concern that can be raised in the current work is whether the recruitment of mostly young adults may have led to results which are not generalizable throughout the life-span. Concerning the hedonic conscious response to touch (pleasantness ratings), it has been shown that, for all ages, the CT optimized stroking velocity (3 cm/s) is experienced as the most pleasant one (Sehlstedt et al., 2016; Croy et al., 2017). As well, the perceived pleasantness of touch has been seen to increase with age (Sehlstedt et al., 2016), leading us to think that with older adults the results of the present work may have been even stronger. Specifically, with older participants satiety to touch may take even more time to occur, and touch is likely an even longer-lasting hedonic experience. However, another study showed no differences in the subjective pleasantness ratings for soft touch in adolescents, young and mature adults (maximum 55 years old) (May et al., 2014), meaning that the stronger hedonic effect of touch possibly occurs in elderly (maximum 82 years old in the study by Sehlstedt and colleagues). Moreover, in paper II one participant was significantly older than the others (66 years old), however she didn´t behave differently in terms of liking and wanting for touch. Concerning paper III and thus the neural correlates to touch, it seems that adolescents show greater activation in posterior insula, inferior frontal gyrus, and striatum in response to soft touch compared to young and mature adults, while these latter two groups exhibit comparable neural activation (May et al., 2014). Knowing this, we may reasonably conclude that no differences in the neural response during long-lasting pleasant touch would have been seen with an older sample. Finally, the broad age range used in paper IV (between 18 and 51 years), and the fact that "age" was used as covariate in the analyses, lead to the observation that the results on heart rate variability are likely generalizable beyond young adults.

4.2 Implications and future directions

The findings may have implications in everyday situations where long-lasting tactile social interactions occur among near ones. For example, caressing and cuddling may lead to a higher level of life quality when prolonged for a rather long time, thanks to its pleasant subjective experience and beneficial physiological (neural and autonomic) effects, which are all positive outcomes that last for a long time. As well, these multiple psychosomatic outcomes of prolonged CT-targeted touch may have clinical implications in long-term touch therapies, for example in the treatment of symptoms of depression or anxiety, commonly associated with autonomic dysregulation, specifically diminished HRV (Thayer et al. 1996; Gorman & Sloan, 2000). A balanced autonomic function in depression and anxiety is crucial, because such diseases are risk factors for cardiovascular issues and cardiac morbidity (Gorman & Sloan, 2000; Kubzansky et al. 1998). Besides clinical settings, long-lasting pleasant touch can be used as a tool for promoting the well-being of the individuals also in terms of massages, because it seems to be not only explicitly rewarding (Lindgren et al., 2014), i.e. “liked”, and desired, i.e. “wanted”, for a long time, but also useful in maintaining a good balance of the autonomic nervous system, crucial for the physiological well-being of the individual.

The present work could be further extended by investigating whether cultural and individual differences potentially modulate the conscious, neural, and autonomic effects of long-lasting pleasant touch. In particular, it would be interesting to explore whether and how touch satiety develops for different groups with a higher or lower degree of tactile exposure, for example due to cultural norms, and a higher or lower degree of touch responsiveness, for example due to individual dispositions. Likewise, it would be interesting to explore the neural and autonomic effects of prolonged touch in such groups.

The conscious and physiological effects of prolonged touch could also be investigated in clinical populations such as those of the autism spectrum, who show touch avoidance (Mammen et al., 2015) and diminished neural response to affective touch (Voos et al., 2013), as well as in individuals with certain personality disorders, for example social anxiety, who exhibit a similar discomfort in response to physical contact (Kashdan et al., 2016).

Finally, a further future direction would also be to explore prolonged touch at a receptor level through microneurography studies in order to investigate peripheral receptor fatigue with repetitive touch over such a long time period. Findings in this field would allow relating CT fatigue to touch satiety.

5. Conclusion

Throughout this thesis we have discovered the multiple outcomes of CT-targeted touch prolonged for times scales longer than several minutes, such as its explicit hedonic effects, and its implicit neural and autonomic effects. Specifically, from paper II, we have seen that long-lasting CT-targeted touch is not easily affected by satiety, thus it is “liked” and “wanted” for a rather long time, especially when the velocity is varied. Furthermore, as documented from paper III, such hedonic effects are accompanied by an increased neural activation in OFC, a region typically involved in the processing of rewarding stimuli. Finally, paper IV demonstrated that the hedonic and neural effects also have autonomic correlates, reflected in the increased HRV in response to pleasant touch. Finally, from paper I we have seen that such long-lasting paradigms were realizable with brush stroking performed through a robotic device because it was equally pleasant as brush stroking produced manually. As well, the use of a robot possibly had the advantage of reducing top down effects, which are more likely to occur in presence of an experimenter delivering the tactile stimulation, and thus allowed the study of the mere CT-related pleasantness perception of touch.

My hope is that this thesis is an important contribution to the study of social affective touch, and that the findings can stimulate future research in this growing and exciting field.

References

Ackerley, R., Backlund Wasling, H., Liljencrantz, J., Olausson, H., Johnson, R. D., & Wessberg, J. (2014a). Human C-tactile afferents are tuned to the temperature of a skin-stroking caress. *J Neurosci*, **34**(8), 2879-2883. doi:10.1523/JNEUROSCI.2847-13.2014.

Ackerley, R., Saar, K., McGlone, F., & Backlund Wasling, H. (2014b). Quantifying the sensory and emotional perception of touch: differences between glabrous and hairy skin. *Front Behav Neurosci*., **8**(34).

Andersson, C., Johnsson, K. O., Berglund, M., & Öjehagen, A. (2009). Measurement properties of the Arnetz and Hasson stress questionnaire in Swedish university freshmen. *Scand J Public Health*, **37**(3), 273-279.

Augustine, J. R., (1985). The insular lobe in primates including humans. *Neurol Res* **7**:2-10.

Barker, D. J., Shepard, P. D., & McDermott, K. L. (1982). Fatigue in cat facial mechanoreceptors. Neurosci Lett, **30**(2), 117-122.

Beck, A.T., & Steer, R.A.(1987). *Beck Depression Inventory–Manual*. San Antonio, TX: The Psychological Corporation.

Berridge, K. C. (1996). Food reward: brain substrates of wanting and liking. Ne*urosci Biobehav Rev*, **20**(1), 1-25.

Berridge, K. C. (2009). ‘Liking’ and ‘wanting’ food rewards: Brain substrates and roles in eating disorders. *Physiol Behav*, **97**(5), 537–550.

Berridge, K.C., & Robinson, T. E. (2003). Parsing reward. *Trends Neurosci* **26**, 507–513.

Bellisle, F., Drewnowski, A., Anderson, G. H., Westerterp-Plantenga, M., & Martin, C. K. (2012). Sweetness, satiation, and satiety. *J Nutr*, **142**(6), 1149S-1154S. doi:10.3945/jn.111.149583

Berntson, G. G., Sarter, M. & Cacioppo, J. T. (1998). Anxiety and cardiovascular reactivity: the basal forebrain cholinergic link. *Behavioural Brain Research*, **94**, 225–248.

Bessou, P., Burgess, P. R., Perl, E. R., & Taylor, C. B. (1971). Dynamic properties of mechano-receptors with unmyelinated (C) fibers. *J Neurophysiol*, **34**(1), 116-131.

Bottorff, J. L. (1993). The use and meaning of touch in caring for patients with cancer. *Oncology nursing forum*, **20**(10), 1531-1538.

Björnsdotter, M., Löken, L., Olausson, H., Vallbo, Å. and Wessberg, J. (2009). Somatotopic organization of gentle touch processing in the posterior insular cortex. *JNeurosci*, **29**(29), 9314-9320.

Björnsdotter, M., Morrison, I., & Olausson, H. (2010). Feeling good: on the role of C fiber mediated touch in interoception. *Exp Brain Res*, **207**(3-4), 149-55.doi: 10.1007/s00221-010-2408-y.

Burgoon, J. K. (1991). Relational message interpretations of touch, conversational distance, and posture. *Journal of Nonverbal Behavior*, **15**(4), 233-259.

Burgoon, J. K., Walter, J. B., & Baesler, E. J. (1992). Interpretations, evaluations, and consequences of interpersonal touch. *Human Communication Research*, **19**(2), 237–263.

Cannon, W. B. (1932). *The wisdom of the body*. Norton, New York.

Carver, C.S., White, T.L., (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scales. *J. Pers. Soc. Psychol.* **67**, 319–333.

Case, L. K., Laubacher, C. M., Olausson, H., Wang, B., Spagnolo, P. A. & Bushnell, M. C. (2016). Encoding of touch intensity but not pleasantness in human primary somatosensory cortex. *J Neurosci*, **36**(21), 5850 –5860.

Cechetto, D. F. (2014). Cortical control of the autonomic nervous system. *Exp Physiol*, **99**(2), 326-331. doi:10.1113/expphysiol.2013.075192.

Chapman, C. E. (1994). Active versus passive touch: factors influencing the transmission of somatosensory signals to primary somatosensory cortex. *Can J Physiol Pharmacol*, **72**(5), 558-570.

Coan, J., Schaefer, H., & Davidson, R. (2006). Lending a hand: social regulation of the neural response to threat. *Psychol Sci*, **17**(12), 1032-1039.

Cole, J., Bushnell, M. C., McGlone, F., Elam, M., Lamarre, Y., & Vallbo, A. (2006). Unmyelinated tactile afferents underpin detection of low-force monofilaments. *Muscle Nerve* **34**, 105-107.

Craig, A. D. (2002). How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci*, **3**(8), 655-66.

Craig, A. D. (2011). Significance of the insula for the evolution of human awareness of feelings from the body. *Ann NY Acad Sci*, **1225**, 72-82.

Croy, I., Luong, A., Triscoli, C., Hofmann, E., Olausson, H. & Sailer, U. (2016). Interpersonal stroking touch is targeted to C tactile afferent activation. *Behavioural Brain Research*, 297,37-40.

Croy, I., Sehlstedt, I., Wasling, H. B., Ackerley, R. & Olausson, H. (2017). Gentle touch perception: From early childhood to adolescence. *Dev Cogn Neurosci*, **S1878-9293**(17), 30023-3. doi: 10.1016/j.dcn.2017.07.009.

Crucianelli, L., Krahé, C., Jenkinson, P. M., Fotopoulou, A. K. (2017). Interoceptive ingredients of body ownership: Affective touch and cardiac awareness in the rubber hand illusion. *Cortex,* **S0010-9452**(17), 30135-1. doi: 10.1016/j.cortex.2017.04.018.

Davidovic, M., Jönsson, E. H., Olausson, H., & Björnsdotter, M. (2016). Posterior superior temporal sulcus responses predict perceived pleasantness of skin stroking. *Front. Hum. Neurosci.*, **10**(432). doi: 10.3389/fnhum.2016.00432.

Deethardt, J.F., & Hines, D. G. (1984). Tactile communication and personality differences. *J Nonverbal Behav*, **8**, 143–156. doi:10.1007/BF00987000.

Dimberg, U. (1990). Facial electromyography and emotional reactions. *Psychophysiology*, **27**(5), 481-94.

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*, **32**(5), 565-574. doi:10.1016/j.psyneuen.2007.03.011.

Drescher, V. M., Whitehead, W. E., Morrill-Corbin, E. D., & Cataldo, M. F. (1985). Physiological and subjective reactions to being touched. *Psychophysiology*, **22**(1), 96–100.

Ebisch, S. J., Ferri, F. & Gallese, V. (2014). Touching moments: desire modulates the neural anticipation of active romantic caress. *Front Behav Neurosci*, **8**, 60.

Essick, G. K., James, A., McGlone, F. (1999). Psychophysical assessment of the affective components of non-painful touch. *Neuroreport*, **10**, 2083-2087.

Etzi, R. & Gallace, A. (2016). The arousing power of everyday materials: an analysis of the physiological and behavioral responses to visually and tactually presented textures. *Exp Brain Res*, **234**(6), 1659-66. doi: 10.1007/s00221-016-4574-z.

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.

Francis, S., Rolls, E. T., Bowtell, R., McGlone, F., O'Doherty, J., Browning, A., & Smith, E. (1999). The representation of pleasant touch in the brain and its relationship with taste and olfactory areas. *Neuroreport*, **10**(3), 453-459.

Funke, F. & Reips, U. D. (2012). Why semantic differentials in web-based research should be made from visual analogue scales and not from 5-point scales. Field Methods, **24**(3), 310-327. https://doi.org/10.1177/1525822X12444061

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

Gard, D.E., 2006. Anticipatory and consummatory components of the experience of pleasure: a scale development study. *J. Res. Pers.* **40**, 1086–1102.

Garnera, B., Phillips, L. J., Schmidt, H.-M., Markuleva, C., O'Connor, J., Wood, S. J., Berger, G. E., Burnett, P. & McGorry, P. D. (2008). Pilot study evaluating the effect of massage therapy on stress, anxiety and aggression in a young adult psychiatric inpatient unit. *Aust. N. Z. J. Psychiatry*, **42**, 414–422. doi: 10.1080/00048670801961131.

Gazzola, V., Spezio, M. L., Etzel, J. A., Castelli, F., Adolphs, R., & Keysers, C. (2012). Primary somatosensory cortex discriminates affective significance in social touch. *PNAS*, **109**(25), E1657-1666. doi:10.1073/pnas.1113211109.

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. doi:10.1002/hbm.21480.

Gorman, J. M. & Sloan, R. P. (2000). Heart rate variability in depressive and anxiety disorders. *American Heart Journal*, **140**, 77–83.

Grewen, K. M., Anderson, B. J., Girdler, S. S., & Light, K. C. (2003). Warm partner contact is related to lower cardiovascular reactivity. *Behavioral Medicine*, **29**(3), 123-130.

Grimm, P. (2010). *Social Desirability Bias* (Vol. 2): Wiley International Encyclopaedia of Marketing.

Hagbarth, K. E., Vallbo, A. B., (1968). Discharge characteristics of human muscle afferents during muscle stretch and contraction. *Exp Neurol* **22**, 674-694.

Harrison, L., Olivet, L., Cunningham, K., Bodin, M., & Hicks, C. (1996). Effects of gentle human touch on preterm infants: pilot study results. *Neonatal Network*, **15**(2), 35-42.

Havermans, R. C., Janssen, T., Giesen, J. C., Roefs, A., & Jansen, A. (2009). Food liking, food wanting, and sensory-specific satiety. *Appetite*, **52**(1), 222-225. doi:10.1016/j.appet.2008.09.020

Havermans, R. C. (2011). "You Say it's Liking, I Say it's Wanting …". On the difficulty of disentangling food reward in man. *Appetite*, **57**(1), 286-294.

Heidt, P. (1981). Effect of therapeutic touch on anxiety level of hospitalized patients. *Nursing Research*, **30**(1).

Henrich, J., Heine, S. J., & Norenzayan, A. (2010). The weirdest people in the world?. *Behav Brain Sci*, **33**(2-3), 61-83. doi: 10.1017/S0140525X0999152X

Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biol Psychiatry*, **54**(12), 1389-1398.

Iggo, A. (1960). Cutaneous mechanoreceptors with afferent C fibres. *J Physiol*, **152**, 337-353.

Jamison, R. N., Gracely, R. H. & Katz, N. P. (2002). Comparison of electronic vs paper VAS ratings: a randomized, crossover trial using healthy volunteers. *Pain*, **99**, 341–347.

Jakubiak, B. K. & Feeney, B. C. (2017). Affectionate touch to promote relational, psychological and physical well-being in adulthood: A theoretical model and review of the research. *Pers Soc Psychol Rev*. **21**(3), 228-252.doi: 10.1177/1088868316650307

Jones, S. E., & Yarbrough, A. E. (1985). A naturalistic study of the meanings of touch. *Commun Monogr*, **52**, 19–56.

Jourard, S. M. (1996). An exploratory study of body-accessibility. *British Journal of Social and Clinical Psychology*, **5**, 221-231.

Jönsson, E. H., Backlund Wasling, H., Wagnbeck, V., Dimitriadis, M., Georgiadis, J. R., Olausson, H., & Croy, I. (2015). Unmyelinated tactile cutaneous nerves signal erotic sensations. *J Sex Med*., **12**(6), 1338-1345.

Kashdan, T. B., Doorley, J., Stiksma, M. C. & Hertenstein, M. J. (2016). Discomfort and avoidance of touch: new insights on the emotional deficits of social anxiety. *Cogn Emot*. **22**, 1-9. doi: 10.1080/02699931.2016.1256867.

Keizer, A., De Jong, J. R., Bartlema, L. & Dijkerman C. (2017). Visual perception of the arm manipulates the experienced pleasantness of touch. *Developmental Cognitive Neuroscience*, in press. https://doi.org/10.1016/j.dcn.2017.09.004.

Kersten, P., Kücükdeveci A.A. & TennantA. (2012). The use of the visual analogue scale (VAS) in rehabilitation outcomes. *J Rehabil Med*, **44**, 609-610.

King, & Bruner. (2000). Social desirability bias: a neglected aspect of validity testing. *Psychol Market*, **17**(2), 79-103.

Kirsch, L. P., Krahé, C., Blom, N., Crucianelli, L., Moro, V., Jenkinson, P. M. & Fotopoulou, A. (2017). Reading the mind in the touch: Neurophysiological specificity in the communication of emotions by touch. *Neuropsychologia*. **S0028-3932**(17), 30198-7. doi: 10.1016/j.neuropsychologia.2017.05.024

Kringelbach, M. L. (2005). The human orbitofrontal cortex: linking reward to hedonic experience. *Nat Rev Neurosci*, **6**(9), 691-702. doi:10.1038/nrn1747.

Kringelbach, & Berridge. (2009). Towards a functional neuroanatomy of pleasure and happiness. *Trends Cogn Sci*, **13**(11), 479-487. doi:10.1016/j.tics.2009.08.006.

Kubzansky, L. D., Kawachi, I., Weiss, S. T. & Sparrow, D. (1998). Anxiety and coronary heart disease: a synthesis of epidemiological, psychological, and experimental evidence. *Annals of Behavioural Medicine*, **20**, 47–58.

Kumazawa, T., & Perl, E. R. (1977). Primate cutaneous sensory units with unmyelinated afferent fibers. *J Neurophysiol*, **40**, 1325-1338.

Kurt, F., Zilles, K., Fox, P. T., Laird, A. R., Eickhoff, S. B. (2010). A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. *Brain Struct Funct*, **214**(5-6), 519-34.doi: 10.1007/s00429-010-0255-z.

Lamm, C., Silani, G., Singer, T., (2015). Distinct neural networks underlying empathy for pleasant and unpleasant touch. *Cortex*, **70**, 79–89.

Lane, J. F. D. (2001). Activity in medial prefrontal cortex correlates with vagal component of heart rate variability during emotion. *Brain Cogn*, **47**(1-2), 97-100.

Light, K. C., Grewen, K. M., & Amico, J. A. (2005). More frequent partner hugs and higher oxytocin levels are linked to lower blood pressure and heart rate in premenopausal women. *Biological Psychology*, **69**(1), 5–21.

Liljencrantz, J., & Olausson, H. (2014). Tactile C fibers and their contributions to pleasant sensations and to tactile allodynia. *Front Behav Neurosci*, **8**(37).

Lindgren, L., Jacobsson, M., & Lamas, K. (2014). Touch massage, a rewarding experience. *J Holist Nurs*, **32**(4), 261-268. doi:10.1177/0898010114531855.

Lindgren, L., Rundgren, S., Winso, O., Lehtipalo, S., Wiklund, U., Karlsson, M., Brulin, C. (2010). Physiological responses to touch massage in healthy volunteers. *Auton Neurosci*, **158**(1-2), 105-110. doi:10.1016/j.autneu.2010.06.011

Löken, L. S., Evert, M., & Wessberg, J. (2011). Pleasantness of touch in human glabrous and hairy skin: order effects on affective ratings. *Brain Res*, **1417**, 9-15. doi:10.1016/j.brainres.2011.08.011.

Löken, L. S., Wessberg, J., Morrison, I., McGlone, F., & Olausson, H. (2009). Coding of pleasant touch by unmyelinated afferents in humans. *Nat Neurosci*, **12**(5), 547-548. doi:10.1038/nn.2312.

Luong, A., Bendas, J., Etzi, R., Olausson, H. & Croy, I. (2017). The individual preferred velocity of stroking touch as a stable measurement. *Physiology & Behavior*, **177**, 129-134.

Mammen, M. M., Moore, G. A., Scaramella, L. V., Reiss, D., Ganiban, J. M., Shaw, D. S., Leve, L. D. & Neiderhiser, J. M. (2015). Infant avoidance during a tactile task predicts autism spectrum behaviors in Toddlerhood. *Infant Ment Health J*. **36**(6), 575–587.

May, A. C., Stewart, J. L., Tapert, S. F. & Paulus, M. P. (2014). The effect of age on neural processing of pleasant soft touch stimuli. *Front Behav Neurosci*, **8**(52). doi: 10.3389/fnbeh.2014.00052

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. doi:10.1093/scan/nsn005.

McDaniel, E. & Andersen, P. A., 1998. International patterns of interpersonal tactile communication: a field study. *Journal of Nonverbal Behavior* **22**, 59–75.

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.

McGlone, F., Wessberg, J., & Olausson, H. (2014). Discriminative and affective touch: sensing and feeling. *Neuron*, **82**(4), 737-755. doi:10.1016/j.neuron.2014.05.001.

McLachlan, C. S., Ocsan, R., Spence, I., Hambly, B., Matthews, S., Wang, L., & Jelinek, H. F. (2010). Increased total heart rate variability and enhanced cardiac vagal autonomic activity in healthy humans with sinus bradycardia. *Proc* (Bayl Univ Med Cent), **23**(4), 368–370.

Meltzoff, A. N. (2007). 'Like me': a foundation for social cognition. *Dev Sci*, **10**(1), 126-134. doi:10.1111/j.1467-7687.2007.00574.x.

Montagu, A., & Matson, F. W. (1979). *The human connection*. New York: Mcgraw-Hill; First Edition.

Morrison, I. (2016). Keep Calm and Cuddle on: Social Touch as a Stress Buffer. *Adaptive Human Behavior and Physiology*, **2**(4), 344–362.

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

Morrison, I., Löken, L.S., Minde, J., Wessberg, J., Perini, I., Nennesmo, I., & Olausson, H., (2011b). Reduced C-afferent fibre density affects perceived pleasantness and empathy for touch. *Brain*, **134**, 1116-1126.

Morrison, I., Löken, L. S., & Olausson, H. (2010). The skin as a social organ. *Experimental Brain Research*, **204**(3), 305-314.

Nasser, J. (2001). Taste, food intake and obesity. *Obes Rev*, **2**(4), 213-218.

Nordin, M. (1990). Low-threshold mechanoreceptive and nociceptive units with unmyelinated (C) fibres in the human supraorbital nerve. *J Physiol*, **426**, 229-240.

O'Doherty. (2004). Reward representations and reward-related learning in the human brain: insights from neuroimaging. *Curr Opin Neurobiol*, **14**(6), 769-776. doi:10.1016/j.conb.2004.10.016

O'Doherty, J., Critchley, H., Deichmann, R., & Dolan, R. J. (2003). Dissociating valence of outcome from behavioral control in human orbital and ventral prefrontal cortices. *J Neurosci*., **23**(21), 7931-7939.

Olausson, H., Cole, J., Valbo, A., McGlone, F., Elam, M., Kramer, H. H., Bushnell, M. C. (2008). Unmyelinated tactile afferents have opposite effects on insular and somatosensory cortical processing. *Neurosci Lett*, **436**(2), 128-132. doi:10.1016/j.neulet.2008.03.015

Olausson, H., Lamarre, Y., Backlund, H., Morin, C., Wallin, B. G., Starck, G., Bushnell, M. C. (2002). Unmyelinated tactile afferents signal touch and project to insular cortex. *Nat Neurosci*, **5**(9), 900-904. doi:10.1038/nn896.

Olausson, H., Wessberg, J., Morrison, I. & McGlone, F. (2016). *Affective Touch and the Neurophysiology of CT Afferents*. New York: Springer. doi:10.1007/978-1-4939-6418-5.

Olausson, H., Wessberg, J., Morrison, I., McGlone, F., & Valbo, A. (2010). The neurophysiology of unmyelinated tactile afferents. *Neurosci Biobehav Rev*, **34**(2), 185-191. doi:10.1016/j.neubiorev.2008.09.011.

Olson, M., & Sneed, N. (1995). Anxiety and therapeutic touch. *Issues in mental health nursing*, **16**(2), 97-108.

Ostlund, S. B., & Balleine, B. W. (2007). The contribution of orbitofrontal cortex to action selection. *Ann N Y Acad Sci*., **1121**(174-92).

Pawling, R., Cannon, P. R., McGlone, F. P., Walker, S. C. (2017). C-tactile afferent stimulating touch carries a positive affective value. *PLoS One*, **12**(3), e0173457. doi: 10.1371/journal.pone.0173457.

Peck, J., Childers, T.L., 2003. Individual differences in haptic information processing: the “Need for Touch” scale. *J. Consum. Res.* **30**, 430–442.

Perini, I., Olausson, H., Morrison, I., (2015). Seeking pleasant touch: neural correlates of behavioral preferences for skin stroking. *Front Behav Neurosci*, **9**(8). doi:10.3389/fnbeh.2015.00008.

Ploner, M., Schmitz, F., Freund, H. J., & Schnitzler, A. (2000). Differential organization of touch and pain in human primary somatosensory cortex. *J Neurophysiol*, **83**(3), 1770-1776.

Pollatos, O., Herbert, B. M., Matthias, E., & Schandry, R. (2007). Heart rate response after emotional picture presentation is modulated by interoceptive awareness. *International Journal of Psychophysiology*, **63**(1), 117–124.

Pope, C. A., 3rd, Verrier, R. L., Lovett, E. G., Larson, A. C., Raizenne, M. E., Kanner, R. E., & Dockery, D. W. (1999). Heart rate variability associated with particulate air pollution. *Am Heart J*, **138**(5), 890-899.

Price, D. D., McGrath, P. A., Rafii, A. & Buckingham, B. (1983). The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain*, **17**, 45–56.

Price, D. D., Staud, R. & Robinson, M. E. (2012). How should we use the visual analogue scale (VAS) in rehabilitation outcomes? II: Visual analogue scales as ratio scales: an alternative to the view of Kersten et al. *J Rehabil Med*, **44**, 800-801.

Putnam, K.M., Pizzagalli, D.A., Gooding, D.C., Kalin, N.H., Davidson, R.J., 2008. Neural activity and diurnal variation of cortisol: evidence from brain electrical tomography analysis and relevance to anhedonia. *Psychophysiology,* **45**, 886–895.

Rapaport, M. H., Schettler, P., & Breese, C. (2010). A preliminary study of the effects of a single session of Swedish massage on hypothalamic-pituitary-adrenal and immune function in normal individuals. *J Altern Complement Med*, **16**(10), 1079-1088. doi:10.1089/acm.2009.0634

Robins, B., & Dautenhahn, K., (2014). Tactile interactions with a humanoid robot: novel play scenario implementations with children with autism. *Int J Soc Robotics*, **6**(3), 397–415. doi:10.1007/s12369-014-0228-0.

Rolls, E. T., & Grabenhorst, F., (2008). The orbitofrontal cortex and beyond: from affect to decision making. *Prog. Neurobiol*. **86**(3), 216–244. http://dx.doi.org/10.1016/j.pneurobio. 2008.09.001.

Rolls, E. T., O'Doherty, J., Kringelbach, M.L., Francis, S., Bowtell, R., & McGlone, F., (2003). Representations of pleasant and painful touch in the human orbitofrontal and cingulate cortices. *Cereb. Cortex*, **13**, 308–317.

Rolls, E. T., Rolls, B. J., & Rowe, E. A. (1983). Sensory-specific and motivation-specific satiety for the sight and taste of food and water in man. *Physiol Behav*, **30**(2), 185-192.

Rolls, E. T., & Rolls, J. H. (1997). Olfactory sensory-specific satiety in humans. *Physiol Behav*, **61**(3), 461-473.

Rolls, B. J., Rolls, E. T., Rowe, E. A., & Sweeney, K. (1981). Sensory specific satiety in man. *Physiol Behav*, **27**(1), 137-142.

Rosier, E. M., Iadarola, M. J., Coghill, R. C. (2002). Reproducibility of pain measurement and pain perception. *Pain*, **98**, 205–216.

Sailer, U. & Ackerley, R. (2017). Exposure shapes the perception of affective touch. *Dev Cogn Neurosci*, **S1878-9293**(17), 30032-4. doi: 10.1016/j.dcn.2017.07.008.

Schaefer, M., Flor, H., Heinze, H. J., & Rotte, M. (2006). Dynamic modulation of the primary somatosensory cortex during seeing and feeling a touched hand. *Neuroimage*, **29**(2), 587-592. doi:10.1016/j.neuroimage.2005.07.016.

Schandry, R. (1981). Heart beat perception and emotional experience. *Psychophysiology*, **18**(4), 483–488.

Schultz, W., Tremblay, L., & Hollerman, J. R. (2000). Reward processing in primate orbitofrontal cortex and basal ganglia. *Cereb Cortex*, **10**(3), 272-284.

Sehlstedt, I., Ignell, H., Backlund Wasling, H., Ackerley, R., Olausson, H. & Croy, I. (2016). Gentle touch perception across the lifespan. *Psychol Aging*, **31**(2), 176-84. doi: 10.1037/pag0000074.

Seth, A. K., Critchley, H. D. (2013). Extending predictive processing to the body: emotion as interoceptive inference. *Behav Brain Sci*, **36**(3), 227-8.doi: 10.1017/S0140525X12002270.

Snaith, R. P., Hamilton, M., Morley, S., Humayan, A., Hargreaves, D., & Trigwell, P. (1995). A scale for the assessment of hedonic tone the Snaith-Hamilton Pleasure Scale. *British Journal of Psychiatry*, **167**, 99 - 103.

Sripongngam, T., Eungpinichpong, W., Sirivongs, D., Kanpittaya, J., Tangvoraphonkchai, K., & Chanaboon, S. (2015). Immediate Effects of Traditional Thai Massage on Psychological Stress as Indicated by Salivary Alpha-Amylase Levels in Healthy Persons. *Med Sci Monit Basic Res*, **21**, 216-221.

Steyer, R., Schwenkmezger, P., Notz, P., & Eid, M. (1997). *Der Mehrdimensionale Befindlichkeitsfragebogen (MDBF)*. Göttingen: Hogrefe-Huber.

Streeter, C. C., Gerbarg, P. L., Saper, R. B., Ciraulo, D. A., & Brown, R. P. (2012). Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. *Med Hypotheses*, **78**(5), 571-579. doi:10.1016/j.mehy.2012.01.021.

Sumioka, H., Nakae, A., Kanai, R., & Ishiguro, H. (2013). Huggable communication medium decreases cortisol levels. *Sci Rep*, **3**(3034). doi:10.1038/srep03034

Suvilehto, J.T., Glerean, E., Dunbar, R.I.M., Hari, R., Nummenmaa, L., 2015. Topography of social touching depends on emotional bonds between humans. *PNAS*, **112**(45), 13811–13816.

Thayer, J. F., Friedman, B. H. & Borkovec, T. D. (1996). Autonomic characteristics of generalized anxiety disorder and worry. *Biological Psychiatry*, **39**, 255–266.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: the neurovisceral integration perspective on self-regulation, adaptation, and health. *Ann Behav Med*, **37**(2), 141-153. doi:10.1007/s12160-009-9101-z.

Ter Horst, G. J., & Postema, F. (1997). Forebrain parasympathetic control of heart activity: retrograde transneuronal viral labeling in rats. *Am J Physiol*, **273**(6 Pt 2), H2926-2930.

Tsakiris, M., Tajadura-Jimenez, A., & Costantini, M. (2011). Just a heartbeat away from one's body: interoceptive sensitivity predicts malleability of body representations. *Biological Sciences*, **278**(1717), 2470-2476.

Triscoli, C., Croy, I., Olausson, H., & Sailer, U. (2014). Liking and wanting pleasant odors: different effects of repetitive exposure in men and women. *Front Psychol*, **5**(526). doi:10.3389/fpsyg.2014.00526

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.doi: 10.1016/j.physbeh.2017.05.006.

Vallbo, A., & Johansson, R. S. (1984). Properties of cutaneous mechanoreceptors in the human hand related to touch sensation. *Hum Neurobiol*, **3**(1), 3-14.

Vallbo, A., Olausson, H., & Wessberg, J. (1999). Unmyelinated afferents constitute a second system coding tactile stimuli of the human hairy skin. *J Neurophysiol*, **81**(6), 2753-2763.

Vallbo, A., Olausson, H., Wessberg, J., & Kakuda, N. (1995). Receptive field characteristics of tactile units with myelinated afferents in hairy skin of human subjects. *J Physiol*, **483**(3), 783-795.

Vallbo, A., Olausson, H., Wessberg, J., & Norrsell, U. (1993). A system of unmyelinated afferents for innocuous mechanoreception in the human skin. *Brain Res*, **628**(1-2), 301-304.

van Boxtel, A. (2010). Facial EMG as a tool for infering affective states. Paper presented a the proceedings of measuring behavior. Eindhoven.

Voos, A. C., Pelphrey, K. A., & Kaiser, M. D. (2013). Autistic traits are associated with diminished neural response to affective touch. *Soc Cogn Affect Neurosci*, **8**, 378-386.

Vrontou, S., Wong, A. M., Rau, K. K., Koerber, H. R., & Anderson, D. J. (2013). Genetic identification of C fibres that detect massage-like stroking of hairy skin in vivo. *Nature*, **493**, 669–673.doi:10.1038/nature11810.

Watson, D., Clark, L.A., Tellegen, A., 1988. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J. Pers. Soc. Psychol.* **54**(6), 1063–1070.

Weiss, S. J. (1990). Effects of differential touch on nervous system arousal of patients recovering from cardiac disease. *Heart Lung*, **19**(5 Pt 1), 474-480.

Wessberg, J., Olausson, H., Fernström, K. W., & Vallbo, A. (2003). Receptive field properties of unmyelinated tactile afferents in the human skin. *J Neurophysiol*, **89**(3), 1567-1575.

Wiklund Fernström, K., Jonsson, H., Wessberg, J., & Vallbo, A. Receptor fatigue and coding of vibration in unmyelinated lowthreshold mechanoreceptors coding tactile stimuli (CT) in human hairy skin. Program No. 154.12. 2002 Neuroscience Meeting Planner. Orlando, FL: Society for Neuroscience, 2002. Online.

Wölk, J., Sütterlin, S., Koch, S., Vögele, C., & Schulz, S. M. (2014). Enhanced cardiac perception predicts impaired performance in the Iowa Gambling Task in patients with panic disorder. *Brain and Behavior*, **4**(2), 238–246.

Zotterman, Y. (1939). Touch, pain and tickling: an electro-physiological investigation on cutaneous sensory nerves. *J Physiol*, **95**(1), 1-28.