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Emotional and physiological responses to touch massage

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Everything that is new or uncommon raises a pleasure in the imagination, because it fills the soul with an agreeable surprise, gratifies its curiosity, and gives it an idea of which it was not before possessed.

Joseph Addison

ABSTRACT

Background: Clinical findings indicate that touch massage has the ability to induce positive emotions and influence stress responses. However, little is known about mechanisms that can explain observed responses.

Aim: To understand mechanisms behind observed emotional and physiological responses during and after touch massage.

Methods: This thesis is based upon healthy volunteers in *Studies I, II, IV* and patients undergone aortic surgery in *Study III*. *Study I* had a crossover design, participants served as their own controls. After randomization they received TM on one occasion and the other occasion served as control. Heart rate variability (HRV), heart rate (HR) saliva cortisol concentration, glucose, insulin in serum and extracellular (ECV) levels of glucose, lactate, glycerol and pyruvat were measured before, during and after TM/control. In *study II*, functional magnetic resonance imaging (fMRI) was used in order to measure brain activity during TM mvement. The study design included four different touch stimulations, human touch with movement (TM movement) human stationary touch and rubber glove with or without movement. Force (2.5 N) and velocity (1.5 cm/s) were held constant across conditions. The pleasantness of the four different touch stimulations was rated on a visual analog scale (VAS-scale). *Study III* had a randomized controlled design. The intervention group received TM and the control group rested. HRV, cortisol, glucose, insulin in serum, blood pressure, oxygen saturation, respiratory frequency and anxiety levels were measured before, during and after TM/control. In *study IV* participants were interviewed about experiences after TM and the text was analyzed by qualitative content analyze.

Results: *Study I*. TM reduced the stress response as indicated by decreased heart rate and decreased activity in the sympathetic nervous system, followed by a compensatory decrease in parasympathetic nervous activity in order to maintain balance. Cortisol and insulin levels decreased significantly after intervention, while serum glucose levels remained stable. A similar, though less prominent, pattern was seen during the control session. There were no significant differences in ECV concentrations of analyzed substances. *Study II*. Human moving touch (TM movement) was significantly rated as the most pleasant touch stimulation. The fMRI results revealed that human moving touch (TM movement) most strongly activated the pregenual anterior cingulate cortex (pgACC). *Studys III*. Self-rated anxiety levels significantly decreased in the patient group that received TM compared with control group. There were no significant differences in physiological stress-related outcome parameters between patients who received TM and controls. *Study IV*. In this study participants talked about the experience of TM in terms of rewards. Expressions like need, desire, pleasure and conditioning could be linked with a theoretical model of reward. Four different categories were identified as wanting, liking, learning and responding.

In conclusion: Results from these studies indicate that receiving TM is experienced as rewarding. Touch massage movement activates a brain area involved in coding of rewarding pleasant stimulations. TM decreases anxiety and dampens the stress response by a decreased activation of the sympathetic nervous activity. Our results indicate that TM is a caring intervention that can be used to induce pleasure, decrease anxiety and stress in the receiver.

Keywords: Touch, touch massage, human touch, stress, anxiety, heart rate variability, fMRI, pregenual anterior cingulate cortex, reward system

ORIGINAL PAPERS

This dissertation is based on the following papers, which will be referred to in the text by their Roman numerals.

I Lindgren L, Rundgren S, Winsö O, Lehtipalo s, Wiklund u, Karlsson M, Stenlund H, Jacobsson C, Brulin C.
Physiological responses to Touch massage in healthy volunteers.
Autonomic Neuroscience: Basic and Clinical 2010 Dec 8; 158 (1-2): 105-10.

II Lindgren L, Westling G, Brulin C, Lehtipalo S, Andersson M, Nyberg L.
Pleasant human touch is represented in pregenual anterior cingulate cortex.
Neuroimage 2012 Jan 1; 59, 3427-32.

III Lindgren L, Lehtipalo S, Winsö O, Karlsson M, Wiklund U, Brulin C.
Touch massage, a complex intervention study.
Nursing in Critical Care. Submitted.

IV Lindgren L, Jacobsson M, Lämås K.
Touch massage in relation to the reward system.
Research in Journal of Clinical Nursing. Submitted.

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ABBRIVATIONS

ACC	Anterior cingulate cortex
ACTH	Adrenocorticotropic hormone
BOLD	Blood-oxygen-level-dependent signal
CRH	Corticotrophin-releasing hormone
dACC	Dorsal anterior cingulate cortex
ECV	Extracellular concentrations
fMRI	Functional magnetic resonance imaging
HF	High frequency
HPA-axis	Hypothalamus-pituitary-adrenal axis
HR	Heart rate
HRV	Heart rate variability
LF	Low frequency
LF/HF ratio	Low frequency and high frequency ratio
OFC	Orbitofrontal cortex
PAG	Periaqueductal grey
PFC	prefrontal cortex
pgACC	Pregenual anterior cingulate cortex
STAI-Y	State-Trait Anxiety Inventory Form Y
TM	Touch massage
VLF	Very low frequency
vmPFC	Ventromedial prefrontal cortex

PREFACE

One of my first experiences of touch massage in clinical practice took place during my work as a specialist nurse in an intensive care unit (ICU). A young man, hurt in a traffic accident, was brought to the ICU with non–life-threatening injuries, but suffering from severe pain and anxiety. His heart rate, arterial blood pressure, and respiratory rate were high and he did not respond to analgesics and sedatives. Finally he was given touch massage, with remarkable results: his heart rate, arterial blood pressure, and respiratory rate decreased and he fell asleep. When he woke up, he said, "Before the massage I was in total pain and anxiety, but during the massage it completely disappeared." My curiosity was aroused, and I wondered what mechanisms could be potent enough to achieve such a positive response? When searching in the literature I realised that there was a dearth of explanation models for how touch and massage affects physiological and emotional mechanisms. This thesis is my attempt to evaluate touch massage systematically and to broaden our knowledge about this care-giving intervention.

INTRODUCTION

In nursing it is well known that interpersonal interactions have an impact on the patient's well-being. It is important that patients feel safe and have confidence and trust in their caregivers. Several caring interventions such as touch massage (TM) are directed at increasing positive, and reducing negative, experiences and feelings. Although nursing research has focused on emotional experiences following touch or massage, little is known about whether and how these experiences can affect other physiological systems. Perhaps the answer is not to separate emotional and physical sensations, but to see the individual as a whole person, in whom different systems interact in complex way. There is a growing body of research and interest in the mind–body interaction, which may be important for nurses and caregivers to understand, as most caring interventions are directed towards improving well-being and reducing aversive stimuli in patients. A current challenge in health care, especially in nursing care, is to use scientific evidence in the treatment and care of patients. Despite the fact that the use of TM has increased over the past decade, no systematic studies of the effectiveness of this treatment have been implemented. The development of new research methods, however, now allows exploration of the potential impact of mental conditions on physiological reactions. Therefore, it is crucial to investigate the effects of TM from a multidisciplinary perspective in order to discover the implications of, and evidence for, using TM in clinical practice.

BACKGROUND

Touch massage

In the western medical tradition, Hippocrates (460-377 B.C.E) found that massage was an important treatment, with several different effects: much rubbing, he suggested, thins the body; moderate rubbing thickens the body; hard massage constricts the tissues, and gentle massage relaxes. Thus different massage techniques could be used for different conditions (Calvert, 2002). In line with Hippocrates thoughts that massage has different effects, focus in this thesis will be on gentle relaxing massage or touch. Classic, hard, Swedish massage and other forms of complementary treatments will not be in focus. The definition of touch massage used in this thesis relies on touch as one of the five senses through which we experience the world. Touch massage is a systematic form of human touch, characterized by gentle touching of the skin with light pressure effleurage and long, slow, calm stroking movements. The pressure is firmer than a casual or accidental brushing, but lighter than classic or Swedish massage. The term "touch massage" in this thesis includes touch, gentle, soft, light, or tactile massage or stimulation and include physiological, emotional, cognitive and social components (Gallace and Spence, 2010, Hertenstein et al., 2009, Loken et al., 2009, McGlone et al., 2007, McCabe et al., 2008, Morrison et al., 2010, Olausson et al., 2010, Rolls, 2010). The label, in our opinion, is not as important as the distinction between hard and soft massage, as they may affect different fibres and receptors in the skin and muscles, which can in turn affect different physiological systems.

Touch in caring

Evolutionary, touch has been suggested as an inherent reward important for reproduction and survival (Grabenhorst and Rolls, 2011). Newborns are usually touched frequently and naturally by their mothers and others in their families and social worlds, and touch has been shown to be important to the development of human and other newborns. Touch can influence weight gain, cognition, stress tolerance, and gene expression in newborns (Claessens et al., 2010, Dunbar, 2008, Field, 2002, Field et al., 2010, Liu et al., 2000, Weaver et al., 2005). Since touch is considered to be so important from both evolutionary and developmental perspectives, it is not surprising that it may also be important in health care. In the late 1800s Florence Nightingale recommended massage in the care of patients, and during that era, it was considered an effective treatment for many of the diseases and conditions for which it may be used today, including stress, insomnia, exhaustion, and constipation (Ruffin, 2011). In nursing, touch is used both as a therapeutic intervention, with the purpose of healing, and also in normal physical contact during bathing, dressing, and other routine care (Routasalo, 1999). Connor and Howett (2009) distinguished between "intentional comfort touch" and non-intentional, procedural, or instrumental touch. Intentional comfort touch is applied with the intention of changing the patient's emotions, for example, holding hands to give some comfort, while instrumental or procedural touch is incidental to physical care and has no intended emotional content.

Intentional comfort touch seems to be important for both health professionals and their patients (Connor and Howett, 2009). Caregivers have described physical contact with their patients as a non-pharmacological, but purposeful, care-giving activity that contributes to a safe, comforting, and pleasing environment (Lindqvist et al., 2012, Edvardsson et al., 2003). Patients have said that touch can enhance their experiences of joy and alleviate suffering, but that it can also be frightening and cause worse suffering (Ozolins, 2011). Therefore, caregivers must be cautious and respectful when touching their patients. In the late 1900s, some nursing research focused on three main aspects of touch: its use; its effects, and patients' experiences. Results from these studies varied, but one consistent conclusion was that touch generally had a comforting and calming effect. (Routasalo, 1999). Touch massage may therefore be both therapeutic and intentionally comforting.

Responses to touch and touch massage

In clinical practice, both mental and physiological responses to touch massage have been observed. This is consistent with prior research; mental responses after touch massage are especially quite similar in patients' descriptions. For example, those who receive touch or touch massage report enhanced positive feelings, such as well-being, pleasure, comfort, relaxation, and confidence (Agren and Berg, 2006, Bergsten et al., 2005, Cronfalk et al., 2009a, Cronfalk et al., 2010, Henricson et al., 2009, Skovdahl et al., 2007). Touch and touch massage also seem to decrease negative emotions such as anxiety, pain, stress, loneliness, and meaninglessness, and to reduce experiences of physiological symptoms (Andersson et al., 2009, Beider and Moyer, 2007, Billhult and Maatta, 2009, Billhult et al., 2008, Cronfalk et al., 2010, Diego et al., 2004, Falkensteiner et al., 2011, Henricson et al., 2008b, Kim and Buschmann, 1999, Lamas, 2011, Lamas et al., 2012, Suzuki et al., 2010). On the other hand, it is difficult to find evidence of the influence of touch and touch massage on physiological stress parameters. Billhult et al. (2009) found that TM lowered systolic blood pressure and heart rate in breast cancer patients, but other studies have conflicting results and researchers request larger sample sizes and clearly designed studies in order to evaluate stress parameters during and after massage (Moraska et al., 2010). Research results therefore indicate that touch massage can affect emotional experiences, and sometimes even physiological parameters, but the question remains, how can these responses be explained?

Existing explanatory models

Various theories have been proposed to explain the observed responses during and after massage (Moyer et al., 2004). One theory is that moderate massage increases activity in the parasympathetic nervous system by activating pressure receptors in the skin (Diego and Field, 2009). Another suggests that the hormone oxytocin is released during touch or massage, and that this hormonal release may explain the observed positive responses (Uvnas-Moberg, 1998). The oxytocin explanation is interesting, but human studies have failed to support it (Billhult et al., 2008, Henricson et al., 2008a, Wikstrom et al., 2003). Moreover, oxytocin's utility as an anti-stress marker has been questioned, because stressful events also contribute to increased oxytocin levels, thus leading to difficulties in interpretation (Semeniken et al., 2009). Although both of these theories are interesting, it remains important to distinguish hard muscle massage from light soft massage, because hard and soft massage might achieve different responses by activating different fibres, receptors, and even different brain regions. Light touch at a force of 0.8 N and a velocity of up to 3 cm/s has been evaluated in terms of pleasantness ratings and brain activity. This kind of touch stimulation was described as pleasant and activated a specific kind of low-threshold unmyelinated mechanoreceptive fibres in the skin, the C-tactile fibres. Sensory information from C-tactile fibres reach a brain area called the insula cortex (Loken et al., 2009, Olausson et al., 2002).

According to these studies, activation of this brain area could eventually explain behavioural, hormonal, and autonomic response during and after slow stroking movements (Craig, 2009, Olausson et al., 2010,). However, although C-tactile fibres are lacking in glabourus (hairless) skin, touch can still be perceived as pleasant even on the palm (Francis et al., 1999b, Kramer et al., 2007), therefore it has to be a complementary explanation (Olausson et al., 2010).

Touch and touch massage in relation to physiological and emotional systems

Few studies have evaluated the relation among human touch (skin-to-skin contact) and brain activation (Kress et al., 2011). To get a broader understanding of the observed responses during and after touch massage, it is perhaps less important to separate emotional and physiological responses than to look at these systems as in constant interaction. Since theories to explain observed responses during and after touch massage are lacking, the following sections will highlight different brain and bodily systems involved in touch and touch sensation. To provide a general understanding of the complexity of these systems, a short section on mind–body interactions is followed by more detailed descriptions.

Mind-body interactions

Today, there is a growing interest in mind-body interactions. New research methods have been developed that makes it possible to evaluate mental experiences in association with physiological processes. According to this view, the brain is the key organ that receives both external sensory input and internal input from the body. Information received by the brain is then integrated with earlier life events, individual genetic differences, and various contextual factors (McEwen, 2008, McEwen and Gianaros, 2011), meaning that the same sensory stimulation can be experienced differently by different individuals and by the same individuals in different contexts. Based on the incoming information, the brain can control and regulate emotion, cognition, behaviour, and physiological responses to adjust the balance in the body (Davidson and McEwen, 2012, McEwen and Gianaros, 2011). The body's ability to maintain balance even while undergoing change, has a large impact on mind-body interaction (McEwen, 2008) and might therefore interact or cooperate with external stimuli.

The skin, the spinal cord, and the brain

Human beings experience the world with their senses and the skin is one of the first senses that develop (Gallace and Spence, 2010). The skin is a particular important sensory organ in the present context. Although, the skin has other functions (protective, endocrine, homeostatic and immunological)(Hertenstein and Weiss, 2011), in this text, the focus will be on its role the skin as a "sensing organ."

The sense of touch allows the perception of pressure, vibration, and texture, and relies upon four different mechanoreceptors in the skin (Pacinian corpuscles, Meissner's corpuscles, Merkel's discs, and Ruffini (McGlone et al., 2007). Tactile impulses travel via Aβ fibres through the dorsal horn in the spinal cord, along the dorsal column pathway, to reach the brainstem. When neurons reach the thalamus, they cross over to the other side, and finally reach the primary and secondary somatosensory cortices (McGlone et al., 2007). Human touch (skin to skin contact) also includes a thermal component and can therefore activate sensory neurons in the skin that encodes thermal stimulation (Hollins, 2010, Rolls et al., 2008).

C-tactile fibres were discovered only a few decades ago. Theses fibres exist only in skin with hair and respond mainly to slow-moving mechanical stimuli at low force (Johansson et al., 1988). It has been suggested that C-tactile fibres contribute to a peripheral touch system conveying emotional feelings (Loken et al., 2009, McGlone and Reilly, 2010). These fibres project to the insula cortex, a brain area of great interest in affective mechanisms (Olausson et al., 2010). Patients lacking Aβ-fibres but with intact C-tactile fibres cannot localize where they have been touched, but they can describe the feeling of touch (Olausson et al., 2002).

Another way to describe the experience of touch in relation to neural activity was presented by Grabenhorts and Rolls (2011). According to their theory, sensory stimulations like touch can be seen as re-inforcers (rewards or punishments) that are processed in reward-related brain areas, such as anterior cingulated cortex (ACC) and orbitofrontal cortex (OFC). The processing in the brain can be divided into three stages. In *Tier 1*, the identity, locality, and intensity of the touch stimulation are processed and brain areas such as the somatosensory cortex and the insula cortex are engaged. In *Tier* 2, the affective or reward value (pleasantness or painfulness) of the touch stimulation is processed. Pleasant and painful touch seems to activate different parts of reward-related brain areas. Touch that is perceived as pleasant seems to be more represented in the medial OFC and pregenual ACC (pgACC), while painful touch is represented in the lateral OFC and dorsal ACC (dACC) (Rolls et al., 2003b). The value or the pleasantness of the touch stimulation can, however be modulated by contextual and cognitive factors (top-down processes). When someone tells us that a lovely, soft, expensive cream is being applied on our arm, the touch stimulation is perceived as more pleasant than when the cream is applied without any label words. This also correlates with neural findings that top-down influences such as label words modulate activity in the OFC and ACC (McCabe et al., 2008). Consciously, top-down modulation engages the prefrontal cortex (PFC), while implicit habit modulation involves the basal ganglia (Grabenhorst and Rolls, 2011). In *Tier 3*, the brain processes adequate responses and actions, i.e. appropriate behaviours and autonomic and endocrine responses, to the perceived pleasant (reward) or painful (punishment) touch (Grabenhorst and Rolls, 2011).

The reward system

The reward-system perspective is interesting as it might explain the pleasure and well-being that is reported during and after TM (Bergsten et al., 2005, Cronfalk et al., 2009a). Rewards in life are important as they make us enjoy and pursue activities particularly important for survival and reproduction, such as eating, drinking, exercising, and having sex. Rolls (2005) proposed that some pleasant perceptions, such as warm touch and sweet taste, are inherited through evolution, gene-specific and unlearned. The social interaction that occurs during touch massage can also have rewarding properties other than the physical touch (Berridge and Kringelbach, 2008). Not all rewards, however, are purely pleasurable sensations; relief from negative stimuli can also be rewarding. As both seeking pleasure and avoiding pain are important for survival, these states affect each other and share some of the same pathways (Leknes and Tracey, 2008, Leknes et al., 2011). For example, expectation of pain relief (the placebo effect) minimizes pain perception and activates reward-related brain areas (Petrovic et al., 2002). Pleasant human touch may also thus activate the reward system through providing pleasure, relief from threat or pain, or a mix of the two.

Berridge and Kringelbach (2011) claim that rewards are active complex processes in the brain that react and code different incoming stimuli, and they describe three major psychological components that are involved in rewards: *liking*, *learning*, *and wanting*.The three components can be conscious or unconscious and engage different brain areas and neurotransmitters. *Liking* is described as the pleasure component of the reward, for example the pleasant sensation of the touch stimulation. *Learning* is the associations and predictions about future rewards based on earlier experiences. *Wanting* is the motivation for obtaining a reward, how much you need and how motivated you are to get the reward (Kringelbach and Berridge, 2009). Some rewards, such as eating and drinking, are homeostatically driven (Berridge, 2004), and motivation for obtaining them is influenced not only by the reward itself, but also by temporary biological states such as appetite, satiety, and stress (Berridge, 2012). Activation of the reward system allows us to enjoy certain stimuli, motivates us, and thereby controls some of our behaviour and bodily responses (Grabenhorst and Rolls, 2011).

Reward system and bodily responses

It is rather well established that social connections such as friendship or family relations influence our physical health, and that social disconnection predicts worse health outcomes (Holt-Lunstad et al., 2010, Miller et al., 2009). However, the underlying mechanisms have only recently begun to be in focus. One theory is that perceived social disconnection activates threat- related brain circuits, while social relations activate reward-related brain areas. These central mechanisms may also have peripheral physiological consequences (Eisenberger and Cole, 2012).

Different emotions seem to affect different brain areas. Pain and threat have, for example, been found to activate the dACC, amygdala and periaqueductal grey (PAG) (Shackman et al., 2011, Eisenberger and Cole, 2012), and some of these brain areas are also involved in social pain, for example dACC (Eisenberger, 2012b). Being disconnected from a close friend or a family member can indeed be hurtful. Experiences of pain and threat can further activate the stress system, and lead to increased heart rate, blood pressure, and respiratory rate. These physiological changes are explained by alterations in the autonomic nervous system (increased sympathetic nervous activity) and alterations in the hypothalamus-pituitary-adrenal (HPA) axis leading to modulated cortisol levels (Medford and Critchley, 2010, Bosch et al., 2009, Roy et al., 2012). The autonomic nervous system and the HPA-axis can further affect activity in metabolic and immune systems, systems that can have both protective and damaging effects. This could in part explain how negative emotions can contribute to illness and increased mortality (Kyrou and Tsigos, 2007, Miller et al., 2009).

On the other hand, caregiving, social support, and skin-to-skin contact can induce feelings of safety and thereby reduce the threat-related responses explained above (Eisenberger and Cole, 2012, Coan et al., 2006, Davidson and McEwen, 2012). One neural explanation of these protective effects could be the association of positive emotions with the activation of reward related brain area, such as subgenual ACC, pgACC, and ventromedial prefrontal cortex (vmPFC) (Roy et al., 2012, Etkin et al., 2011, Grabenhorst and Rolls, 2011). Some researchers also claim that the reward system has the potential to dampen incoming threatening stimuli. This is supported by results showing a negative correlation between activity in reward-related brain areas (pgACC and vmPFC) and activation in PAG and with sympathetic activity (Etkin et al., 2011). Furthermore, endorphins released through rewarding stimuli are associated with reductions of both sympathetic nervous and HPA activity (Eisenberger, 2012b). The proposal that positive and negative experiences affect different areas of the brain correlates well with the results from a study comparing different touch stimulations. Painful and pleasant touch activated different part of ACC. Painful touch activated the dACC, a part of the brain associated with negative emotions (Rolls et al., 2003a, Shackman et al., 2011), while pleasant touch activated the pgACC, a reward-related brain area involved with threat inhibition and positive emotions (Rolls et al., 2003a, Rolls et al., 2003b, Etkin et al., 2011).

Although the brain influences other peripheral physiological systems, these systems can in turn influence the brain. This two-way communication facilitates an optimal balance between different systems even when external circumstances are changed. Prolonged stress can, however, disturb that balance (McEwen and Wingfield, 2010). The challenge is to find effective medications to treat the condition, because drugs that restore balance in one physiological system may affect others, contributing to even more imbalance (McEwen, 2008). Interventions designed to promote well-being are therefore important since well-being might change neural and endocrine activity, leading to a reduced stress response (Davidson and McEwen, 2012, McEwen, 2006). Rewarding stimuli may thus influence bodily balance (McEwen and Gianaros, 2011) and TM might be an important intervention that helps the body to heal itself.

AIMS OF THE THESIS

General aim

The general aim was to understand the mechanisms involved in emotional and physiological responses observed during and after TM.

Specific aims

- To evaluate the physiological effects of TM on stress responses in healthy volunteers.

- To evaluate human moving touch (TM) in respect to brain activity and ratings of pleasantness in healthy volunteers.

- To evaluate the effects of touch massage on levels of anxiety and physiological stress in patients that has undergone elective surgery.

- To describe and analyse healthy individuals' expressed experiences of TM.

METHODS

Research design

Since the overall aim of this thesis was to evaluate both emotional and physiological responses to touch massage, an interdisciplinary approach was applied. A mixed-method design and methodological triangulation, including both quantitative outcome parameters and qualitative data, was used to evaluate mind–body interactions. In synthesizing the results, triangulation was useful to create a holistic entirety of the various data sets (Jick, 1979, Ostlund et al., 2010).

A schematic overview of the four different studies is presented in Table 1. In *Studies I, II,* and *III,* hypothetico-deductive approaches were used. The hypothesis in *Study I* was that TM could reduce stress response by increasing parasympathetic nervous activity. This study had a cross-over design, and the participants served as their own controls and participated on two separate occasions. In *Study II,* we tested the hypothesis that human touch with movement could elicit a specific response in brain areas coding for pleasant experiences. In this study a within-subject block design was used. The hypothesis in *Study III* was that TM could decrease anxiety and stress response in patients who had undergone elective aortic surgery, and for this study a randomized controlled design was applied. S*tudy IV* had a qualitative design with an abductive approach. Unlike the hypothetico-deductive approach, the theoretical stand point from which the data were analyzed was not present during study preparation, data collection or in the initial data analysis. After reading the text, the assumption that participants talked about experiences of TM in terms of rewards were evaluated.

Table 1. A schematic overview of the studies in this thesis.

Study	Design	Measurements	Participants	Mean age (standard deviation)
I	Quantitative Cross-over design	HRV Cortisol Glucose Insulin Microdiasysis	22 healthy volunteers	28.2 (6.4)
II	Quantitative Within-subject, block design	fMRI Pleasantness ratings	16 healthy volunteers	30.2 (8.2)
III	Quantitative Randomised controlled design	STAI HRV Blood pressure Respiratory rate Saturation Cortisol Glucose Insulin	20 patients scheduled for aortic surgery	65.9 (5.1)
IV	Qualitative design	Interviews Qualitative content analysis	15 healthy participants	43.4 (14.8)

Participants

Study I. In response to advertisements in local newspapers and on bulletin boards, and to verbal requests, 63 volunteers applied to participate in the first study. Inclusion criteria were no tobacco use, no medication (except one woman who used oral contraception), and no disease. Thirty-six volunteers met the inclusion criteria and out of these, 22 healthy participants (11 male and 11 female) (Table 1) were randomly selected.

*Study II***.** In response to advertisements in a local newspaper and verbal requests, 30 volunteers applied to participate in the second study. This study took place in an MRI environment and the exclusion criteria were any metallic object inside the body, pregnancy, claustrophobia, head injury, and psychiatric or neurological disorder. After screening, 16 individuals participated in the study (8 male and 8 female) (Table 1).

Study III. All patients planned for aortic surgery in Umeå Hospital between October 2009 and June 2011 was invited to participate. Of 32 individuals, 27 agreed to participate, seven of whom were excluded due to postoperative complications. A total of 20 individuals participated in the study (16 male and 4 female) (Table 1). All participants in this study had cardiovascular diseases and took hypertensive medications; there were no overall between-group differences in medications or diseases.

Study IV. Through an advertisement on the homepage of the website of a qualified tactile massage therapist, 15 people (2 male and 13 female) applied to participate (Table 1). The participants had different life situations; some lived alone, and some lived in a relationship. They also had various professions and some were on sick leave. Two of the participants suffered from chronic pain.

Data collection

Outcome parameters

Clinical experiences of TM indicated reduced anxiety and increased well-being in the receiver, as well as decreased heart rate, blood pressure, and respiratory rate. The chosen outcome parameters were therefore related to these previously observed responses (Table 1).

Heart rate variability (HRV)

In order to evaluate effects of TM on the autonomic nervous system and its influence on the sinus node, HRV was used. HRV refers to beat-to-beat fluctuations in heart rate (HR). Heart rate reflects the average level of autonomic nervous system activity, while HRV reflects the variation. The parasympathetic nervous system can quickly adjust the time for the next heart beat, whereas the sympathetic nervous system is slower in regulating heart beats. This reaction discrepancy in reaction times creates variability i different frequencies. Parasympathetic nervous activity is mainly within the high frequency region (HF: 0.15–0.40 Hz), whereas the low frequency region (LF: 0.04–0.15 Hz) is mediated by both sympathetic and parasympathetic nervous activity. Fluctuations in the very low frequency region (VLF: ≤0.04 Hz) are not fully understood but have been suggested to reflect thermoregulation and activity in the renin–angiotensin system. The LF/HF ratio reflects the sympatho/vagalbalance. (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). HRV data were sampled from five electrodes of an electrocardiography (ECG) device connected to a monitor (Marquette Solar 8000M monitor, GE Healthcare, Milwaukee, USA). Data were stored on a computer for analysis by custom-made software. Mean values of HR and HRV indices were calculated for five-minute baseline segments starting every 20 minutes. HRV was analysed by power spectrum analysis. RR intervals were converted to time series, and ectopic beats and missing data were replaced by interpolation. The power spectral density was estimated using auto-regressive modelling. The following

HRV indices were calculated for each five-minute segment: total power in the frequency region of 0.003 to 0.50 Hz (Ptot), and the power of the very low frequency (P_{VLF}), low-frequency (P_{LF}), and high-frequency (P_{HF}) components. All HRV analyses were performed using Matlab (Mathworks Inc., Natick, Ma., USA). In *Studies I* and *III* heart rate (HR) and heart rate variability (HRV) were sampled before, during, and after TM or control.

Blood pressure, respiratory rate, and oxygen saturation

Blood pressure, oxygen saturation, and respiratory rate were measured non-invasively as stress indicatora**.** Data was collected from a monitor (Marquette Solar 8000M monitor, GE Healthcare, Milwaukee, USA) connected to a software computer system (Picic, Critical Care Manager, care suite 8.2, Wakefield, UK). Measurements were taken before and after intervention or control in Study III.

Saliva and serum cortisol concentrations

To evaluate the effect of TM on changes in the HPA- axis, cortisol was measured in *Studies I* and *III*. The HPA axis has a feedback system of corticotrophin-releasing hormone (CRH) from the hypothalamus that activates adrenocorticotropic hormone (ACTH) in the pituitary; ACTH is then transported via the blood stream to the adrenal glands, stimulating cortisol secretion that in turn inhibits the release of CRH (Berne, 2004). In *Study I*, free cortisol concentrations in saliva were measured using saliva collection tubes (Salivette, Sarsted, Nűmbrecht, Germany) and analysed using Spectria Cortisol RIA (Orion Diagnostica, Finland). The purpose was to measure saliva cortisol concentrations in both studies. However, in *Study III* the participants did not have enough saliva, so serum cortisol concentrations were analysed instead, although they reflected the bounded cortisol level. Serum cortisol samples were collected preoperatively from a venous catheter (18 G 32 mm Smiths Medical, Milano, Italy) and postoperatively from an arterial catheter (20 G 1.10 × 45 mm, Becton Dickinson, Singapore) and analysed using Roche reagents on a Cobas 6000/8000 analyser. The cortisol samples were collected at the same time of day in each study. In *Studies I* and *III* samples for saliva and serum cortisol analyses were collected before and directly after TM or control. Additionally, in *Study III* serum cortisol samples were collected on the evening of the study day and the following morning.

Serum insulin and serum glucose concentration

To evaluate TM's effect on glucose metabolism, serum insulin and glucose concentrations were measured in *Studies I* and *III*. Samples were collected from a venous catheter (18 G 32 mm Smiths Medical, Milano, Italy) in Study I and from an arterial catheter in Study III (20 G 1.10 × 45 mm, Becton Dickinson, Singapore). The glucose samples were analysed using Ortho Vitros GLU slides on a Vitros 5.1 FS analyser and insulin samples were analysed using Roche Elecsys Insulin reagents on a Modular E170 analyser. Samples were collected before, during, and after TM and control. In *Study III* samples for analyses of glucose and insulin concentrations were also collected later in the evening and the morning after the study day.

Microdialysis

In *Study I,* microdialysis was used to monitor local glucose metabolism in the tissue. The microdialysis technique is designed to measure local metabolic changes in different tissues (Abrahamsson, 2010). Extracellular fluid was sampled by a catheter placed in the abdominal adipose tissue. In this study we used microdialysis catheters (CMA 60, CMA Sweden) with a membrane length of 30 mm and a cut-off of 20 kDa. The catheters were connected to a microdialysis-pump (CMA 107, CMA Sweden) and perfused with Ringer solution at a rate of 1.0 µl/minute. The microvials (CMA, Sweden) were changed every 20 minutes and the dialysate was analysed with colourimetric analysis (CMA 600, CMA Sweden). The catheter remained inserted through the study time and the small microvials (placed outside the body) were changed every 20 minutes, measuring extracellular (ECV) concentrations of glucose, pyruvate, lactate, and glycerol before, during, and after TM and control.

State-Trait Anxiety Inventory Form Y (STAI-Y)

To evaluate TM’s effect on self-rated anxiety the Swedish version of STAI-Y instrument was used. The STAI-Y measures state-anxiety as a temporary condition of anxiety and trait-anxiety as a long-term condition. The instrument has good construct validity, as well as reliability for internal consistency and test-retest. STAI-Y has been used for several years and in different disciplines and contexts. In *Study III* the state-anxiety STAI-Y was used to evaluate immediate changes in anxiety levels on a 20 items rated on a 4-point response scale. The items were summarized into a total score ranging from 20 to 80, with higher scores reflecting higher levels of anxiety (Spielberger, 1972, Spielberger, 1983). The participants rated their anxiety levels before and after TM or rest.

Functional magnetic resonance imaging (fMRI)

To evaluation of brain activity in relation to touch stimulations in *Study II*, fMRI method was used. The fMRI method is a non-invasive technique that measures brain activation by detecting changes in blood flow while a subject performs an experimental task or receives some kind of stimulation during scanning. Neurons that are activated consume more oxygen, causing the blood flow to increase in response to the increased oxygen demand. Hemoglobin (oxygen transporter) in the blood has different magnetic properties depending on whether it carries oxygen or not. These changes in oxygenation can be recorded when interfering with the magnetic field of an MRI scanner. The blood-oxygen-level-dependent (BOLD) signal provides an estimate of changes in neural activity (Huettel et al., 2008). In *Study II*, data from the fMRI scanning was collected using a 3.0 T General Electric Discovery MR750 whole-body MRI system. Functional T2*-weighted images were collected EPI-sequence (field of view=248×248 mm;

matrix=96×96; 37 oblique axial slices; slice thickness=3.9 mm; repetition time=2 s; echo time=0 ms; flip angle=80°). The fMRI images were pre-processed and analysed using Statistical parametric mapping (SPM) (The Wellcome trust centre for neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm) with a batch function in an inhouse program (DataZ). Prior to the analysis, the images were corrected for slice timing and then realigned and unwarped to compensate for head movements during scanning. The images were then normalized to a standard anatomic space (Montreal Neurological Institute standard brain) and finally spatially smoothed using an 8 mm full-width at half-maximum isotropic Gaussian kernel.

Pleasantness rating

In order to evaluate the pleasant experience of touch stimulations (touch massage) in *Study II*, we used a VAS-scale, on which −5 was very unpleasant, 0 was neutral, and +5 was very pleasant. A similar scale was used in a related study that evaluated pleasant touch (Rolls et al., 2003b). The participants rated the pleasantness before fMRI scanning.

Interviews

In *Study IV*, data collection was conducted directly after the second TM session in qualitative research interviews. Each interview lasted between 10 and 45 minutes. The interviews were semi-structured and the guide included the following questions: How was your experience of TM? What expectations did you have before TM and how well were those expectations fulfilled? What influenced the massage experience? Have you experienced any long-term effects of TM? The interviews were tape recorded and later transcribed.

Procedure for intervention and data collection

Intervention

TM was given in all studies; however, the length of TM differed in *Study II* from the other studies because the research method required short stimuli sessions. The intervention in this study is referred to as human moving touch. All massage therapists had been trained in the Takti Pro method (Ardeby, 2007), which is a specific pattern of long and slow moving touch stimulations over the skin. Circular movements were performed on the fingers and toes and neutral oil was used in all studies. The specific pattern applied helped the different masseurs to perform similar movements. The pressure applied can be described as lighter than classic massage but harder than a casual brush. However, to examine the pressure and velocity during touch massage (Takti Pro), a customized touch device was constructed. The interventions are described in more detail under the respective studies.

The touch device

The device constructed to evaluate the force and velocity applied during TM had a dummy arm with a force transducer built in. The force and velocity used in TM was measured at 2.5 N and 1–5 cm/s, respectively. The researcher was trained to apply similar stimulations with both hands using a display which showed the perpendicular forces at the two arms, respectively. The dummy arm rested on a stand, which measured the perpendicular and the tangential forces applied (Figure1).

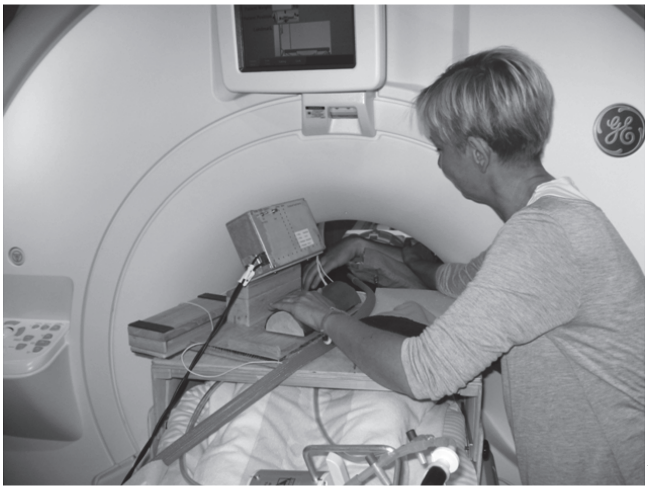
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Figure 1. The touch device in the scanner room indicated the different touch conditions, the correct force (2.5 N) and the correct velocity (1–5 cm/s). The force of the mirror movement applied on the dummy arm was measured by force transducers and sampled in a computer.

Procedure and intervention

Study I. Took place between March and November 2008. As this study had a cross-over design, the participants were randomized to start with either a control or an intervention session by sequential numbers in opaque envelopes. Both sessions (TM and control) took place at the same time of day. The participants were prepared with catheters (microdialysis and peripheral venous catheters) two hours before TM or control to avoid experience of any pain during the study. Physiological outcome parameters were sampled (Table 1) before, during and after TM or control. In the TM session participants received TM on hands and feet for 80 minutes (20 min/body part). The setting was prepared with candles and soft music. During the control session the participants rested in the same setting. After the TM or control session the participants rested for additional 20 minutes.

Data were collection in *Study II* during August and September 2010. The study was performed in an MRI setting and partly within an MR scanner. A touch device constructed for this project could evaluate force/pressure and velocity used when performing TM. The force was measured at 2.5 N and the velocity 1-5 cm/s. This information was then used when evaluating TM movement in the scanner. The TM movement in this study is referred to as human moving touch. In order to have a tight comparison, three other touch stimuli were also applied. Human stationary movement and rubber glove with and without movement. Before scanning the participants rated the pleasantness of the four different touch stimuli. When placed in the scanner, the four touch stimulations were applied for 20 s each and repeated six times in a block design (20 s on and 20 s off). The different touch stimulations were balanced applied guided by the touch device and a data program special constructed for the study. The researcher applied touch stimulation by sliding the palm of the right hand over the patient's right forearm in the distal direction, while simultaneously using the left hand to perform a similar but mirrored movement on a dummy arm with similar frictional to the real arm (Figure 1). The device indicated the pressure and velocity during the different touch stimulations so that these variables could be held constant. The device sampled data that later could be correlated with fMRI data.

Data collection for *Study III* was carried out between October 2009 and June 2011. The participants were block randomized to either control or intervention using numbers in opaque envelopes. Before surgery, stress-related outcome parameters were collected to measure baseline levels. After surgery the researcher visited the participants every morning until they were neurologically, cardiovascularly, and respiratorily stable. When participants were stable they either received TM or they rested under similar circumstances and in the same setting. Participants in the intervention group received TM on hands, arms, legs, and feet for 60 minutes. Outcome parameters were collected before, during, and directly after TM or control. In addition, blood samples were collected later that evening and on the morning after.

Study IV was carried out from September to November 2010. The participants in this study received TM on two separate occasions. A whole body TM was given to the participants (feet, legs, back, neck, head, stomach, arms and hands) for 60 minutes. The setting was prepared with candles and soft music. There was no control group in *Study IV*. To capture the immediate feeling of TM, the interviews were conducted directly after the second occasion in a separate room.

Data analysis

Statistics

In *Study I*, if data were positively skewed they were log-transformed before analysis. Repeated measures ANOVA were used to analyse variables before, during, and at follow-up after TM or control session. Comparisons versus baseline were done using a simple contrast. Paired sample t-test was used to test for differences between TM session and control session at each time point. Data from the microdialysis samples were negatively skewed and therefore Wilcoxon signed rank test was used. A $p<0.05$ was considered significant in all tests.

In *Study II*, Wilcoxon sign rank test was used to test for differences between pleasantness ratings in the four touch stimulations, and after a Bonferroni correction, $p<0.01$ was considered significant. A linear regression was made to create a beta-value-image for each condition. The beta-value-images were thereafter used to create beta-contrasts that were subsequently statistically evaluated in group tests by one-sample t-tests. A two (material: human hand/rubber glove) by two (stimulation: stationary/moving) factorial ANOVA was used to test for main and interaction effects. The alpha level for main and potential interaction effects was $p_{FWE}<0.05$. In the planned contrast for moving human hand relative to the other three touch stimulation a voxel threshold of $p_{unc}<0.005$ with a cluster threshold of 50 was used.

In *Study III***,** non parametric tests were used for ordinal data, Wilcoxon rank test for within group comparisons and Mann-Whitney U to test for differences between groups. Alpha level for the non parametric test was stated to $p<0.01$ after Bonferroni correction. When interval data were repeatedly measured, a parametric, mixed between–within subjects' analysis of variance was conducted. Skewed data were log-transformed and tested for normality. Because of the tests sensitivity and recommendation, $p<0.001$ was considered significant (Pallant, 2005).

Qualitative content analysis

The interviews conducted in *study IV* were subjected to qualitative content analysis. After reading the text, the researchers discussed the content and formed reasoned inferences. The empirical findings indicated that the participants talked about their experiences of TM in terms of rewards, so the researchers studied the literature in this area. In light of the knowledge gained from the literature and guided by this perspective, the texts were then re-read and the aim extended to describe experiences of TM in relation to the reward system. A reward model described by Berridge and Kringelbach (2008) was found applicable for this purpose and used both as a categorizing tool and as a theoretical standpoint. According to this reward model, three psychological components can be identified: *wanting*, *liking*, *and learning*. The interview text was then categorized according to these components. The model is described in more detail in the Background section of this thesis. The analysis was an iterative process and alternated between empirical findings and the theoretical standpoint and the model (Raholm, 2010).

Ethical considerations

Ethical approval for the project was given by the Regional Ethical Review Board in Umeå (Dnr 07-183M). All participants received an introductory letter with a brief description of the study and an invitation to participate. Those who were interested in participating received another letter with more detailed information. All participants were also verbally informed and assured that their participation was voluntary and that they could leave the study at any time with no recrimination (*Studies I–IV*). Persons scheduled for aortic surgery were invited to participate in *Study III*. The invitation to participate was issued before surgery, thus avoiding the possible influence of medication on their decision to participate or not. All participants signed a written consent. Only the research group had access to personal data. Furthermore, all data material was encoded; names mentioned in *Study IV* are all fictive. The massage therapists were educated in the TaktiPro method, and this education includes instruction about having respect for individuals and being responsive to the participants' needs.

RESULTS

Study I

Results from study I revealed that there was a significant decrease in HR after 5 min (p= 0.003) that lasted for 65 minutes in the massage session. This pattern was similar in the control session but the decrease was significantly more pronounced during the TM session (Figure 2). At the end of TM and rest HR returned to baseline in both sessions.

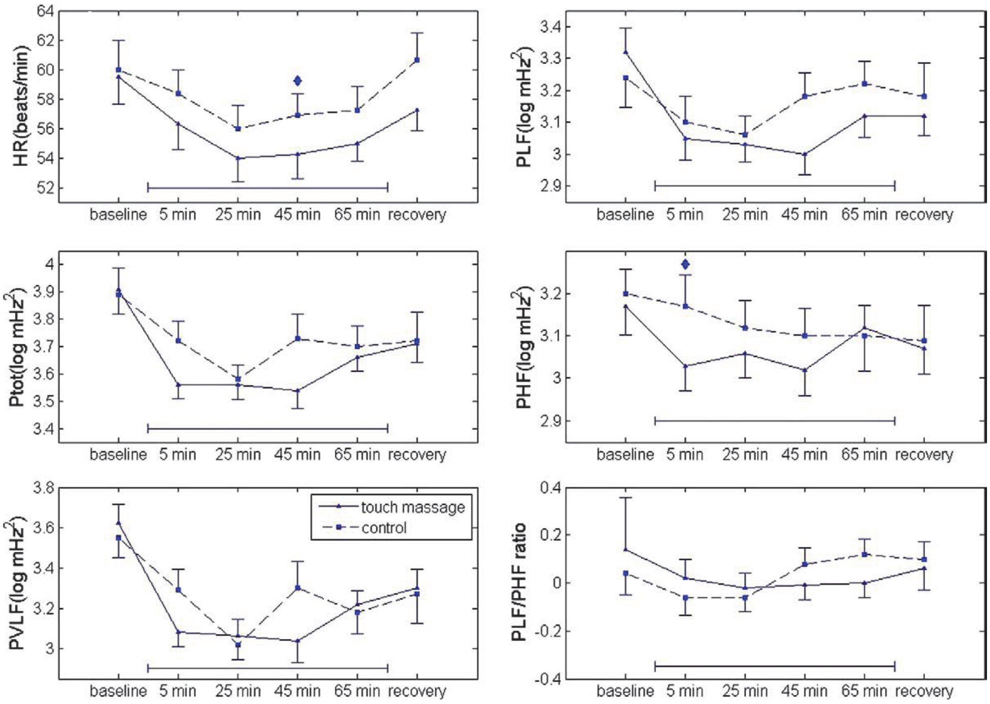

Figure 2. Heart rate and HRV components measured before, and every 20 minutes during TM/control. The line under the curve represents intervention time. # denotes differences between TM and control session. The left panel shows heart rate (HR), total HRV (ptot), and VLF components. In the right panel are LF, HF components and LF/HF ratio are presented.

The trend analysis for all HRV components revealed a similar biphasic pattern to that shown in the HR component. Total HRV decreased after 5 min (p=<0.001) and for 65 min in the TM session (Fig 2). In the control session a significant decrease appeared after 25 min (p=0.005).

In the HF component, reflecting parasympathetic nervous activity, there was a significant decrease after 5 min (p=0.008) in the TM session while a significant decrease was shown at the end of the control session (p=0.023) (Fig 2).

In the LF component reflecting both sympathetic and parasympathetic nervous activity, there was a significant decrease after 5 min in the LF component ($p<0.001$) in the TM session and no significant difference over time in the control session (Fig 2).

In the TM session a decrease in the VLF component from the baseline level was significant for the whole session (Fig 2), while in the control session significant decreases occurred only after 25 minutes and at the end of the session (Fig 2). The VLF components have been suggested to reflect thermoregulation and activity in the renin–angiotensin system.

After 10 minutes, the ratio between LF and HF showed a significant decrease from baseline levels in the TM session ($p=0.024$). The decrease lasted for 20 minutes and was close to one (close to zero in log scale), indicating balance between the LF and HF. In the control session there was no significant difference from baseline level (Fig 2).

There were significant differences in saliva cortisol and serum insulin concentrations overtime, but not between sessions (TM/control) (Table 2). No significant differences were observed in serum glucose concentrations or concentrations of glucose, lactate, pyruvate, and glycerol in ECV.

Table 2. Saliva cortisol, serum insulin and glucose concentrations before, immediately after and 1 hour after TM/control. *denotes significant differences within groups from baseline value (p<0.05)

			Baseline			**After**				**1 h after**			
			mean	SD	n	mean	SD	n		mean	SD	n	
Cortisol	nmol/L	massage	12.0	8.8	/21	5.7	3.6	/21	*	5.5	5.1	/20	*
Cortisol	nmol/L	control	13.9	13.0	/22	7.0	7.8	/22	*	5.6	3.2	/21	*
Insulin	mIU/L	massage	21.0	17.8	/22	5.5	3.2	/21	*	5.0	4.3	/22	*
Insulin	mIU/L	control	19.8	13.7	/22	5.1	3.0	/21	*	5.5	6.5	/22	*
Glucose	mmol	massage	4.4	1.0	/22	4.6	0.5	/21		4.4	0.6	/22	
Glucose	mmol	control	4.5	0.8	/22	4.6	0.4	/22		4.4	0.6	/21	

Study II

The results from study II revealed that human moving touch was rated significantly more pleasant than the three other touch stimulations; human stationary touch (p=0.002) and rubber glove, with and without movement (p<0.001) (Figure 3).

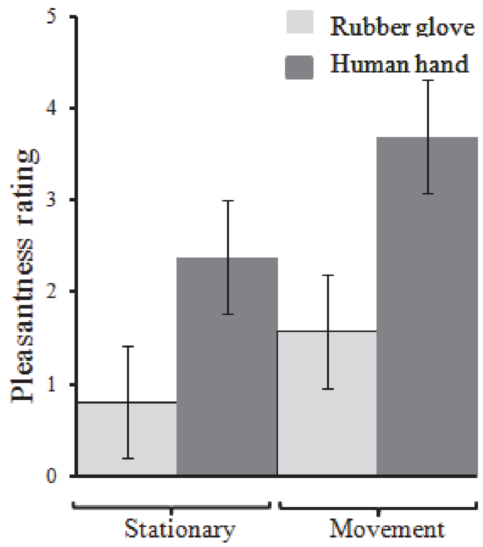

Figure 3. Results of the pleasurable ratings of the four different touch stimulations revealed that human moving condition was rated as most pleasant.

In comparison of human moving touch condition with the other three touch conditions, the fMRI results revealed a significant effect in the bilateral insular cortex. This effect was however strongest for both moving conditions, while the human moving touch condition gave the strongest response in the pgACC (Figure 4).

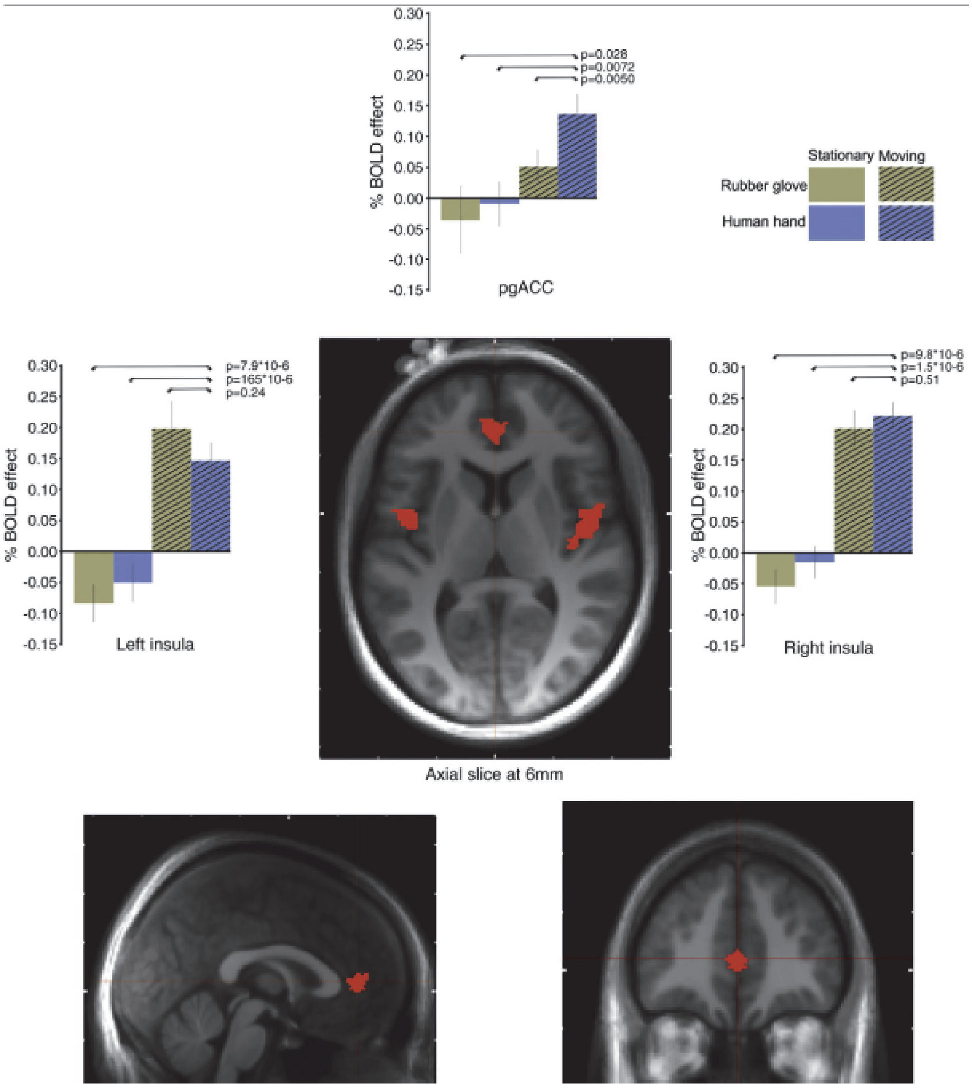

Figure 4. BOLD-profiles for the different touch stimulations rubber glove stationary, hand stationary, rubber glove with movement and hand with movement are shown in a bar diagram for each cluster. Right and left insula (right insula x,y,z=52, −26, 18,cluster size, cs=2290, z=5.21; left insula x,y,z=−44, −32, 20, cs=655,z=5.32) and ACC (x,y,z=0, 42, 4, cs=127, z=3.16.) mean over voxels in cluster. Error bars indicate s.e.m. Above the bars, p-values indicate the significance of the paired t-tests of moving human hand against each of the other three conditions.

A significant main effect for the moving versus stationary stimulations was observed in the bilateral insular cortex (x,y,z=46,−30, 24, cs=1676, z=7.96; x,y,z=−60,−22, 18, cs=612,z=6.35) and contralateral somatosensory cortex (x,y,z=28,−38, 70). Moreover, a main effect of material (rubber glove and human hand) was found in the cerebellum (x,y,z=8, −42, 24, cs=585, z=5.53) in which the rubber glove achieved a greater BOLD signal. (An incidental finding revealed when checking for outliers was that three participants did not recruit activity in pgACC; these same participants reported high stress levels during the study). In summary, the human moving touch was rated some the most pleasant touch stimulation and most strongly activated the pgACC.

Study III

There was a significant decrease in anxiety levels measured by STAI-Y scores after TM in the intervention group (p=0.007), but not in the control group (p=0.833). There were significant differences between the TM group and the control group in the level of STAI-Y before (p=0.007) and after (p=0.001) TM or rest (Table 3).

Table 3. Anxiety levels and stress related outcome variables are presented as mean and standard deviation before and after TM/control.

		Before TM/control									**After TM/control**					
		8.00 pm			**11.30** pm			**1.30** am			**7.00** pm			**8.00** am		
		n	*mean*	*SD*	*n*	*mean*	*SD*	*n*	*mean*	*SD*	*n*	*mean*	*SD*	*n*	*mean*	*SD*
Cortisol/s[a]	Control	10	591.0	330.3	10	558.4	244.3	10	465.8	283.5	10	633.9	311.1	9	567.4	374.1
	TM	10	521.1	252.6	10	443.3	169.5	9	539.2	181.3	10	466.9	221.8	10	614.2	187.2
Insulin/s[b]	Control	10	27.2	13.9	10	37.0	15.9	10	41.8	33.6	10	49.7	47.6	10	32.7	26.1
	TM	10	37.0	15.4	10	56.5	26.8	9	35.9	21.4	9	53.0	31.8	9	42.8	24.1
Glucose/s[c]	Control	10	7.2	1.8	10	7.8	1.8	9	7.8	2.2	10	8.3	2.6	10	7.0	2.3
	TM	10	6.8	1.7	10	7.2	1.8	10	6.5	1.3	10	7.7	2.0	10	7.1	2.2
SBP[d]	Control				10	132.8	17.7	10	134.7	19.8						
	Tm				10	124.9	15.3	10	124.3	13.5						
DBP[d]	Control				10	65.4	11.9	10	65.1	13.4						
	TM				10	55.0	11.9	10	67.9	15.7						
RF[e]	Control				10	17.7	4.8	10	19.2	4.7						
	TM				10	18.9	6.8	10	15.6	7.5						
Oxygen Saturation[f]	Control				10	96.2	2.7	10	96.1	2.1						
	TM				10	95.7	1.8	10	96.3	1.2						
STAI-Y[g]	Control				10	46.4	8.6	10	46.6	11.0						
	TM				10	35.6	5.9	10	27.4	7.1						

SBP= Systolic blood pressure, DBP= Diastolic blood pressure, RF= Respiratory frequency and STAI-Y= State-Trait Anxiety Inventory Form Y.
[a] nmol/L, [b] mIU/L, [c] mmol, [d] mmhg, [e] /min, [f] %, [g] totscore

There were no significant differences in the other stress related outcome parameters (systolic and diastolic blood pressure, respiratory rate, oxygen saturation, serum cortisol, insulin and glucose concentrations or HRV components)

Study IV

Participants in *Study IV* talked about their positive experiences of TM in term that could be used in context of the reward system. The three psychological components of the reward model were identified in the text. In the *wanting* category, participants talked about a desire and need for human touch and TM. They talked about human touch as essential and impossible to live without, and said that TM could satisfy that need. Participants also said that when they were under severe pressure their need for touch was more pronounced. In the *liking* category, participants expressed feelings of pleasure, comfort and, happiness after having TM. These descriptions were often related to safety and relaxation and TM was described as a "dose of sedatives." In the *learning* category the informants talked about contextual and interpersonal factors that could modulate their experience of receiving TM. Repeated TM sessions increased the pleasure in what was described as "a process where the body and mind learned to recognize the TM." Stress could influence the experience of TM in two ways; if the participants were stressed before TM, it took them longer to relax, but if they received TM before a stressful event, they tolerated the stress better afterwards. Participants who suffered from pain said that TM altered their affective experience of pain, so that although they still felt it, they did not care so much about the pain. Participants also talked about conditioning, describing how they become relaxed as soon as they entered the room where the TM was performed. A fourth component was also identified in the text. This category was named *responding* because the participants often talked about their responses after TM. These responses were described as altered mental and physical conditions that could be rewarding in themselves. For example, increased bodily awareness, diminished cognitive control, and increased emotional feelings were all experienced as pleasant conditions.

DISCUSSION

In the first section the separate studies are briefly reviewed and a tentative synthesis of results from the four different studies follows.

Result discussion

Study I

In line with clinical observations, results from *Study I* indicated that TM had the ability to reduce activity in the stress system. Contrary to our hypothesis and earlier results (Diego and Field, 2009, Delaney et al., 2002), the reduced stress response was not associated with increased parasympathetic nervous activity; instead we found decreased sympathetic nervous activity *and* decreased parasympathetic nervous activity. The reduced parasympathetic activity during TM was interpreted as a compensatory effect in order to maintain autonomic balance (Lindgren et al., 2010). Looking at the two branches of the autonomic nervous system in relation to each other, it would be uneconomic to have the two systems working only in opposite directions when they could compensate for each other sometimes by acting synergistically (Paton et al., 2005, Wiklund et al., 2000). However, the autonomic nervous system is complex and the interpretation of HRV results can be difficult. Therefore it is rather important to report all of the HRV components so that the reader can follow the interpretations made. For example, in one case, a decreased HRV could be interpreted as reduced parasympathetic nervous activity and increased stress response. But in this case, the HR component was also reduced, making such an interpretation illogical. We did not find any significant changes in other outcome parameters in this study. The reduced cortisol levels over time during both TM and control were probably associated with the normal daily variations due to the circadian rhythm (Karatsoreos and McEwen, 2011). Using stress related outcome parameters based on glucose metabolism was difficult, since the body has the capacity to compensate for changes by up- and down-regulating different systems, stress related changes can be difficult to capture (McEwen, 2000, McEwen and Gianaros, 2010).

Study II

The results from *Study II* showed that human moving touch was rated as the most pleasant in comparison with the other three touch stimulations (human stationary touch and rubber glove, with and without movement), and the fMRI results revealed that human moving touch (TM) most strongly activated pgACC (Lindgren et al., 2012). This result is consistent with results from other studies evaluating pleasant touch and warm stimulation of the skin (Rolls, 2010, Rolls et al., 2003b). Furthermore, pgACC is a part of the reward system and proposed to be involved in affective coding of incoming stimuli, particularly the coding of *pleasant* stimulations (Grabenhorst and Rolls, 2011). C-tactile fibres in the skin have been found to respond to light forces (0.8N) and slow stroking movements and to engage the insular cortex. This pathway has been described as conveying positive emotional experiences (Loken et al., 2009, McGlone and Reilly, 2010, Morrison et al., 2009). We also found increased activity in the insular cortex during moving touch stimulations; however, this activation did not differ whether the movement was performed by a human hand (skin-to-skin) or by a glove, indicating that it is the movement *per se* that is coded for represented in this brain area. According to Grabenhorst and Rolls´s theory, one explanation might be that insula activation is further processed in the OFC and ACC, where the valuation of the reward is performed (Grabenhorst and Rolls, 2011).

Study III

Participants in *Study III* receiving TM reported significantly less anxiety than the control group. This is in line with clinical findings and with results from other massage studies (Campeau et al., 2007, McVicar et al., 2007, Noto et al., 2010, Moyer et al., 2004, Garner et al., 2008). The anxiety levels were initially lower in the TM group than in the control group. This might partly be explained by anticipation, since participants were informed whether or not they would receive TM before they rated their anxiety levels. It has been proposed that expectation can be an important component of different complimentary methods and may activate similar limbic brain areas (Esch et al., 2004). However, anxiety levels significantly decreased after TM, while there was no such change in the control group. In future studies it would be interesting to measure anxiety levels both before and after information in order to evaluate the effect of anticipation. There were no significant differences observed in other stress-related outcome parameters. This could be caused by low sample size and large intra-individual variability, but also by the fact that the surgery in itself can trigger a stress response (Banz et al., 2011). It is difficult to carry out intervention studies; there are several confounders to be taken into account, and intervention studies are time-consuming (Campbell et al., 2007). Therefore, a complex intervention guideline was used for discussion the discussion of the methods and results (Craig et al., 2008).

Study IV

In *Study IV*, the participants talked about their experiences after TM in terms of positive, pleasurable, and hedonic feelings. These descriptions of massage experiences have also been described in other studies (Agren and Berg, 2006, Billhult and Maatta, 2009, Billhult et al., 2007, Bredin, 1999, Cronfalk et al., 2009b, Henricson et al., 2009, Lamas et al., 2012). Our interpretation was that these experiences were associated with rewards. Using a reward model as a categorizing tool we could link the interview text to the three different psychological components of the reward system: *wanting*, *liking*, and *learning* (Berridge and Kringelbach, 2008), supporting the assumption that TM activates the reward system. Furthermore, a fourth category, labelled *responding*, was described in which the participants talked about how TM could alter their bodily and mental states. For example, participants described how TM could diminish their cognitive control, which led to a release of emotions. Although both positive and negative feelings arose, the experiences even of the negative feelings were described as pleasant. This was also found by Mazzeo, who found that participants reported that they came in contact with their emotions after massage and that they felt a sense of relief and well-being along with the emotions (Mazzeo, 2008). TM was also described as increasing the participants' sense of bodily awareness, and this state too was experienced as something pleasant. In people whose body image is skewed, massage seems to improve it (Hart et al., 2001).

The participants said that they wanted and needed human touch, especially during times of sad or negative events, and that TM could satisfy this need. Other researchers found that touch in caring is experienced as comforting and calming (Routasalo, 1999) and patients who have been touched have a positive experience of their hospitalization (Henricson et al., 2009). It has been proposed that touch and sweet taste are inherent rewards necessary to survival and reproduction (Grabenhorst and Rolls, 2011) and some participants said that their body cried out to be touched, which is similar to the need for any other rewards. Participants described how contextual and interpersonal factors could alter the pleasant feelings of touch and either enhance or dampen the experience. When looking at rewards in general, cognitive components can affect how much a reward is liked, and cultural and social norms can influence how we experience certain events (Leknes and Tracey, 2008). This could partly explain why the view and acceptance of touch differs between different cultures and societies (Gallace and Spence, 2010). When children are taught that touch is something shameful, their experience of touch may alter.

A tentative synthesis of the results

In this section, results from the four different studies are discussed in relation to each other. This discussion is not intended to be an explanation of the observed responses during and after TM. The purpose is instead to create a new hypothesis that can be further tested in the future.

Hypothesis

The results from the four different studies are summarized and interpreted as follow: TM induces pleasure within the receiver and activates reward-related brain areas (pgACC). The activated brain area has a high density of opioid receptors, and one possibility is that TM affects endogenous endorphins. It has also been proposed that pgACC is part of a brain circuit important for emotion regulation, which could partly explain the decreased anxiety levels in participants after TM. Activation of the reward-related brain area further influences the stress system by modulating autonomic nervous activity. In addition, cognitive (contextual and interpersonal) factors seem to modulate the experiences of TM

Discussion of the hypothesis

Since positive emotions seem to affect our health, it is important to increase our knowledge about the underlying mechanisms in order to utilize the body´s own resources to heal itself. Perhaps caring interventions such as TM or human touch are more important than we could imagine. Although some research links negative emotions like depression, fear and pain with alteration in the autonomic nervous system and HPA-axis, the research into how positive emotions influence health is sparser. Nevertheless, there is a growing body of research that has focused on how social interactions and positive emotion may promote well being (Eisenberger and Cole, 2012, Davidson and McEwen, 2012, McEwen and Gianaros, 2011). Some researchers have made a connection between the reward system and positive health outcome (Eisenberger, 2012a).

Although, touch is a peripheral sensory stimulation, it is in the brain the affective coding is represented, how we experiences the touch stimulation (Grabenhorst and Rolls, 2011). When talking about pleasant versus painful touch, it is reasonable to take the reward system into consideration. Rewards like pleasure are motivational, while fear and pain contribute to caution, all in order to improve our chances of survival and reproduction. Human touch is a complex reward, since pleasant touch can be seen as both a rewarding sensory physical stimulation and a social interaction reward (Grabenhorst and Rolls, 2011, Berridge and Kringelbach, 2008). These two components cannot be separated and thus they are both included in the concept of human touch and TM. TM might also activate the reward system in two different ways, as both a pleasant sensation and as a relief from negative stimuli (Leknes et al., 2011). This is confirmed by the participants in *Study IV*, who described TM as a pleasurable sensation that also reduced pain and anxiety (*Studies III* and *IV*). Similar results have been found in other studies (Bergsten et al., 2005, Cronfalk et al., 2009b, Billhult and Maatta, 2009, Goodfellow, 2003). The suggestion that pleasant human touch or human moving touch activates the reward system is supported by results from *Study II*, in which pgACC was most strongly activated by human moving touch. This brain area is also activated during positive emotions, such as happiness or optimism (Sharot et al., 2007, Etkin et al., 2011, Vogt, 2005, Roy et al., 2012). Furthermore, in *Study IV*, the participants described experiences of TM that could easily be linked to reward-related words, such as need, desire, pleasure, and conditioning.

Another interesting question is what kind of transmitter or transmitters are involved in pleasant experiences. In *Study IV* the participants said that during TM it felt like a “dose of sedatives.” According to Kringelbach and Berridge, the liking component or the pleasure component in the reward system is influenced by endorphins (Kringelbach and Berridge, 2009). This fits well with the fact that the pgACC area contains a high density of opioid receptors (Vogt, 2005) and is activated both by morphine and endorphines. It also fits with Dunbar´s idea that endorphins, among other transmitters, are released during social bonding (Dunbar, 2008). The participants from *Study IV* who suffered from pain, described that TM did not alter the intensity of pain, but that the pain became bearable, indicating that TM could modulate the affective component of pain (Vogt, 2005). However, there are probably several transmitters involved in this process.

Our finding that TM reduces anxiety is supported by several other studies conducted in different patient groups (Campeau et al., 2007, McVicar et al., 2007, Noto et al., 2010, Moyer et al., 2004, Garner et al., 2008). It is remarkable that a simple human touch can have such impact on anxiety. However, considering touch from an evolutionary view, it is not so surprising. In 1958, Harlow studied infant monkeys who were allowed to choose between a synthetic surrogate mother who fed them and a warm, soft surrogate mother with no food. He found that monkey infants preferred the warm and soft mother, especially when they were searching for comfort (Harlow, 1958). One interesting finding in this project was that the STAI instrument used in *Study III* in order to evaluate anxiety levels has been shown to correlate negatively with pgACC activity (Klumpp et al., 2011, Krug and Carter, 2010). This is supported by findings from *Study II and III*; TM reduces anxiety scores and increases pgACC activity. Furthermore, the pgACC and the vmPFC have been proposed to be important brain circuits involved in emotion regulation and have the ability to dampen incoming threatening signals (Etkin et al., 2011). It is reasonable to assume that exposure to stressors over the long term may the affect protective brain areas (pgACC and vmPFC) (McEwen and Gianaros, 2011, Etkin et al., 2011), as was supported by one incidental finding in our fMRI study. Three participants did not recruit activity in the pgACC area during TM stimulation, although they rated the touch stimuli as pleasant. The same three participants also reported high levels of stress (Lindgren et al., 2011). This is admittedly a small group, but the findings converge with studies showing that individuals suffering from stress and PTSD syndrome fail to recruit activity and have grey matter reduction in the pgACC (Etkin and Wager, 2007, Kasai et al., 2008). In line with this finding, participants from our qualitative study *(Study IV)* reported that it took them a longer time to relax if they were stressed before they received TM, but if they had massage before a stressful event, they found that their tolerance levels increased. TM could thus be a valuable intervention, promoting well-being and dampening negative input.

Although, TM can modulate feelings and emotions, the physiological stress responses measured by blood pressure, cortisol, glucose and insulin concentration etc. were more difficult to capture. We did, however, found alteration in the autonomic nervous system in healthy participants. The autonomic nervous system is thought to be correlated with emotions; increased sympathetic nervous activity is supposed to correlate with negative emotions and enhanced parasympathetic nervous activity with positive emotions (Thayer and Brosschot, 2005, Porges, 2007). Earlier studies that have evaluated massage in relation to the autonomic nervous system have found increased parasympathetic nervous activity during massage (Diego and Field, 2009, Delaney et al., 2002). In contrast and surprisingly, our results revealed decreased sympathetic and decreased parasympathetic nervous activity during TM (Lindgren et al., 2010). Nevertheless, the sympathetic reduction in *Study I* may be neural explained by results from *Study II*, because increased activity in the pgACC has been suggested to correlate negatively with sympathetic nervous activity (Etkin et al., 2011, Beissner et al., 2012). However, the brain and autonomic nervous system interaction is complex (Medford and Critchley, 2010) and there might be other explanations.

When newborns cry, touch can be very comforting to them but it has also been shown that touch stimulation, social interaction and maternal care are important for development of emotional, cognitive processes and weight gain (Champagne et al., 2003, Liu et al., 2000, Feldman et al., 2010, Field, 2002, Field et al., 2010, Landers and Sullivan, 2012, Fox et al., 2011, Nelson et al., 2007). In animal studies, a high degree of tactile stimulation early in life protects against stress later in the adulthood (Liu et al., 1997, Francis et al., 1999a). Although, touch in early childhood is found to be very important, it seems to become less important over the lifetime. Some people do not even like to be touched. It is clear that individual differences exist and that cultural and contextual factors can modulate the perception of sensory stimulations and emotion (Rolls, 2005, Roy et al., 2012). Physical touch can, for example, be either erotic stimulation or friendly contact depending on who is the toucher. In some cultures and societies human touch is totally accepted, while in others touch is seen as something shameful (Gallace and Spence, 2010). Participants in *Study IV* also said that contextual and personal factors could either enhance or reduce their positive experience of TM.

Emotions can be regulated by cognitive abilities (Ochsner et al., 2012). The reward system can be modulated and the needs can be enhanced or inhibited (Leknes and Tracey, 2008). One interesting finding was that participants reported increased emotional feelings and diminished cognitive control during and after massage (*Study IV*). This is also supported by results from other studies (Mazzeo, 2008). It is possible that bottom-up signals may modulate top-down cognitive control. This is an interesting notion, as increased cognitive control can be important in some mental diseases, while in others there is a need to minimize cognitive control and get in touch with the emotions.

Methodological discussion

Study III partly focused on methodological issues and the British Medical Research Council (BMC) framework was used as a guideline to discuss and reflect upon difficulties when conducting complex interventions such as TM. Thus, study III improved our knowledge in how to design and evaluate interventions in clinical praxis.

Study IV had a qualitative design with an abductive approach (Raholm, 2010). Since several other studies have reported similar results for the experience of TM, with the participants often describing positive feelings during and after TM, our intention was to obtain a deeper insight into *one* of several perspectives. We have tried to make the analysis process as open as possible while related to a model, so that the reader could follow the interpretations we made. The reward model that we used in the analysis was based on psychology and neuroscience and our data were based on described experiences. The different approaches could be an advantage as the different approaches points in the same directions (Jick, 1979). In *Studies I-III*, hypothetico-deductive approaches were applied in which we tried to falsify our hypotheses; in some cases, we failed to falsify them, which means that those hypotheses are a provisional truth. With this approach, however, there is a risk to rejecting the truth even if it exists, simply by having too small sample sizes that may contribute to Type 2 errors.

The sample size (fifteen participants) in *Study IV* was an ordinary size for other qualitative interview studies (Kvale and Torhell, 1997) as the participants´ experiences were quite similar. Although the sample sizes in *Studies I-III* were relatively small, significant differences were detected, which could indicate that the effects were quite strong. *Study I and II*, had a within-group design, the participants were their own controls, which makes the sample sizes more appropriate than in *Study III* that had a between group design (Mills et al., 2009). Randomized and controlled designs are the gold standard but even this design is not perfect for evaluating caring and complex interventions (Blackwood, 2006). Caring interventions are often time- and personnel- consuming; furthermore, the risk of losing participants and measurements make it difficult to include enough individuals. Another problem in conducting randomized controlled studies is the blinding process, which is impossible in intervention studies such as TM. In *Study III*, we chose between having a larger sample including different patient groups or having a homogenous patient group with fewer individuals. Both decisions have their limitations. Although a larger sample sizes can make it easier to find significant differences between groups, there is also more confounders to take into account.

The outcome parameters that showed significant differences, HR and HRV components in *Study I* and anxiety levels in *Study III* exhibited the same pattern in all individuals, indicating that the differences would have been larger with a larger sample size. In *Study III*, there were large inter- individual differences in all the physiological outcome parameters. This could be due to several internal and external factors affecting the measured outcome parameters. The microdialysis used in *Study I* was not useful for this project because changes in local tissue was far from the outcome that we were interested in. In contrast, fMRI was a useful research method that contributed greatly to the purpose of this thesis.

A main problem in this project was the influence of the music in *Study I and IV*. Retrospectively, music should not have been included at all in these studies, since music in itself can reduce stress (Nilsson, 2009) and therefore influence the results. In *Study I* the music component was not a strong bias as it was present in both sessions, and only the intervention differed. In *Study IV*, there is a possibility that the music either enhanced or dampened the experience of TM. However, in the interviews, when the participants talked about factors that could affect their experiences and music was mentioned as one contextual factor, so to a certain extent this was part of the result. Another difficulty in the project was that different parts of the body were massaged in the different studies; however the force and velocity were similar. The choice of body parts partly depended on practical issues, for example ECG- recording for HRV sampling made it impossible to massage some body parts. The human factor has been discussed as a possible bias in massage studies, but we suggest that the human and interpersonal component is a part of TM, not a confounder. Nevertheless, the interpersonal component can probably enhance or dampen the experiences during massage.

Clinical implication

In clinical practice, it is important to find treatments to relieve stress in patients. Stress can be caused both by physiologic reactions to illness and by feelings of powerlessness in life-threatening situations. Using TM as a complementary treatment could be one way to reduce stress and maintain health; in cases of illness, TM could serve as a complementary treatment to restore health by reducing pain, anxiety, and sleep disturbance. Thus, the use of sedatives and analgesics might be reduced and the side effects of drugs be avoided. In a long-term perspective, the length of stay in hospital might also be shortened. Through TM, patients are given the opportunity to focus their attention on themselves, and to feel seen and acknowledged. Because positive emotions have been shown to have health benefits, well-being becomes important from a biomedical, as well as a psychological perspective, and TM and human touch can thus be used in easy and important caring interventions.

This project has brought insight to some practical issues regarding TM. It seems that the pleasantness of TM increases after repeated sessions. For stress reduction, a length of 30 minutes is preferable, but it might take longer for a stressed receiver to relax. The pressure used in TM is 2.5 N ("lighter than classic and Swedish massage, and harder than a brushing movement") and the movement should be slow (1–5 cm/s). It is important to remember that contextual factors can either enhance or dampen the TM experience. TM is a valuable complement to other treatments in order to reduce stress, pain and anxiety in patients.

Future research

In future research it would be interesting to conduct a pharmacological fMRI study with the aim of evaluating whether human moving touch (TM) releases endorphins in reward-related areas of the brain. Since research about human touch in relation to brain activation is sparse, there are several interesting studies that could be conducted and insights to be gained in mind–body interactions

CONCLUSIONS

- TM reduced the stress response as indicated by decreased heart rate and decreased activity in the sympathetic nervous system, followed by a compensatory decrease in parasympathetic nervous activity in order to maintain balance. TM did not influence the HPA-axis or glucose metabolism in healthy volunteers.

- TM movement/moving human touch were rated as most pleasant among studied stimuli (human touch with and without movement and rubber glove with and without movement). The fMRI results revealed that TM movement most strongly activated the pgACC.

- TM reduced anxiety levels in patients who had undergone elective aortic surgery, but did not reduce stress related parameters in these patients.

- TM was experienced positively. These experiences could be linked to reward expressions such as, desire, need, pleasure and conditioning suggesting that TM influences the reward system.

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"You must remember, family is often born of blood, but it doesn't depend on blood. Nor is it exclusive of friendship. Family members can be your best friends, you know. And best friends, whether or not they are related to you, can be your family." Trenton Lee Stewart
To my big family, thank you!

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Populärvetenskaplig sammanfattning på svenska

För att minska stress, oro och ångest hos patienter används ofta lugnande eller smärtstillande medel som kan förlänga vårdtiden på grund av bieffekter. Oberoende av vetenskaplig evidens används ibland touch massage (TM) som en komplementär behandling för att minska stress, oro och ångest. TM är en form av långsam och mjuk massage som omfattar huden, medan traditionell massage även omfattar underliggande muskulatur. I klinisk praxis har patienterna berättat att de blivit lugnare och mått bra av TM. Dessutom har blodtryck, hjärt- och respiratorisk frekvens sjunkit under tiden patienterna fått TM, vilket tyder på positiva effekter på såväl känslomässiga upplevelser som kroppens stressreaktioner. I dagsläget saknas det förklarings modeller om hur dessa effekter uppstår. Syftet med denna avhandling var därför att utvärdera emotionella och fysiologiska effekter av TM.

I första delstudien utvärderades om TM kunde minska fysiologisk stress hos friska frivilliga individer. Tjugotvå deltagare fick delta i studien vid två olika tillfällen. Vid det ena tillfället fick de TM och vid det andra tillfället fick de vila i samma miljö. Provtagning och mätning av stressrelaterade markörer genomfördes före, under och efter TM/vila. Resultatet visade en signifikant sänkning av hjärtfrekvensen över tid i TM gruppen. Liknande mönster kunde registreras i kontrollgruppen men signifikant mindre uttalad. Sänkningen av hjärtfrekvensen berodde på minskad aktivitet i det sympatiska nervsystemet som följdes av en kompensatorisk sänkning av det parasympatiska nervsystemet i syfte att bibehålla den autonoma balansen.

I den andra delstudien utvärderades hur hjärnan påverkas av mänsklig beröring med rörelse (TM rörelse). Sexton friska frivilliga försökspersoner fick skatta upplevd behaglighet av fyra olika beröringar; mänsklig beröring med rörelse (TM rörelse), mänsklig beröring utan rörelse, rörelse med handske, och handske utan rörelse. De fyra olika stimuleringarna utvärderades även med hjälp av funktionell magnetkamera (fMRI). Resultatet visade att försökspersonerna skattade mänsklig beröring med rörelse (TM rörelse) som mest behaglig. Dessutom visade fMRI resultatet att den mänskliga beröringen med rörelse starkast aktiverade ett specifikt område i hjärnan (pregenual cingulate cortex). Detta hjärnområde aktiveras vid belöning och är involverat i känsloreglering. Dessutom innehåller hjärnområdet ett stort antal morfin receptorer som aktiveras vid morfin tillförsel och vid frisättning av kroppseget endorfin.

I tredje delstudien utvärderades effekten av TM på fysiologisk stress och ångest hos patienter som var inlagda för att operera ett planerat aorta aneurysm. Tjugo patienter blev randomiserade till att antingen få TM eller vila. Mätningar och provtagning skedde före, under och efter TM respektive vila. Resultatet visade att patienter som fått TM skattade ångest signifikant lägre efter TM än de som endast vilade.

I fjärde delstudien fick femton friska deltagare TM under två tillfällen. Direkt efter andra tillfället intervjuades deltagarna om upplevelsen av att få TM. Deltagarna kände ett behov och en längtan efter mänsklig beröring som TM tillfredsställde. TM gav välbehag, njutning och avslappning men upplevelsen påverkades positivt eller negativt beroende av förhållanden i omgivningen. Känslan av välbehag ökade i takt med antalet TM. Deltagarnas upplevelser kopplades till en belönings modell som skiljer mellan att vilja ha (wanting), tycka om (liking), att lära sig (learning). Förrutom dessa tre kategorier skapades en fjärde kategori som handlade om att TM förändrade känslomässiga och kroppsliga tillstånd (responding) som i sig upplevdes som belönande.

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