Are the antidepressive effects of massage therapy mediated by restoration of impaired interoceptive functioning? A novel hypothetical mechanism

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ABSTRACT

Interoception is an individual person’s sense of the physiological condition of his/her entire body. Recent research has shown that depression is associated with impaired interoceptive accuracy. Treatments that can improve disturbed interoception are scarce in clinical practice and could complement established therapies. Accumulating evidence suggests that massage therapy significantly alleviates symptoms of depression. However, the mechanisms underlying these effects have remained unclear. We are going to propose a novel mechanism linking these antidepressive effects to a massage-induced modulation of interoceptive states. Particularly affective massage therapy applies slow, rhythmic, and caress-like touch that stimulates C tactile (CT) afferents in the non-glabrous skin. CT mediated touch elicits responses in interoceptive brain areas (e.g. the insular cortex) that have been associated with abnormal interoceptive representations in depressed subjects. Thus, we hypothesize that antidepressive effects of massage therapy are mediated by restoration of the impaired interoceptive functioning through stimulation of CT afferents or related interoceptive structures. If our proposed mechanism is valid, massage is probably one of the most ancient interoceptive treatments.

Introduction

Major depressive disorder (MDD) is one of the most common mental disorders with an estimated age-standardized point prevalence of 4.1–4.7\% [1] and a cumulative lifetime risk of 14.6\% for high-income [2]. Females are more prone to develop MDD, with women having a roughly twofold higher risk compared to men [2]. Depression is a highly recurrent mood disorder [3] that gives rise to chronicity in 15\% of all affected subjects [4]. According to data of the Global Burden of Disease Study, depression is the leading cause of disability attributable to mental disorders [5] and ranks third among all leading causes of disability worldwide [6]. Symptoms of depression also occur as a comorbidity in diseases other than MDD, e.g., cancer, Parkinson’s disease, inflammatory bowel disease or pain conditions [7–10]. Thus, depression is of significant public health relevance and challenges the medical care system [11].

Pharmacotherapy and psychotherapy are currently the state-of-the-art treatments for the management of depression. Nevertheless, use of complementary and alternative medicine (CAM) for depression is widespread especially in the U.S. [12,13]. Main reasons for using CAM were negative experiences with conventional medical treatments like adverse effects or non-response to various treatments [14]. Survey data suggest that manual therapies like massage or acupressure are preferred by depressed subjects using CAM treatments [14]. While most CAM procedures lack any scientific proof of their efficacy accumulating evidence exists that massage therapy alleviates symptoms of depression as well as anxiety, pain, and perceived stress [15–19]. Whereas one review which focuses exclusively on four RCTs having applied classical Swedish massage claimed insufficient evidence for antidepressive or anxiolytic effects of massage [20], an older meta-analysis concluded that the effect size of massage therapy in depression is moderate to large and comparable to those of psychotherapy [17]. In hospitalized MDD patients using a randomized cross-over-design, it could be clearly shown that massage therapy is superior to a relaxing non-touch control situation [21]. Positive effects of a combination of mindfulness practice and touch therapy have also been shown in moderately depressed patients [22]. Massage therapy also alleviates comorbid depression in different medical conditions, such as acquired immune deficiency syndrome [23], breast cancer [24], chronic fatigue syndrome [25] or dementia [26]. Antidepressive and anxiolytic effects of massage
therapy have also been shown in the perinatal period [27,28]. Meta-analytic evidence suggests that multiple sessions of massage therapy have the largest effects on depression. Some reviewers concluded that two treatments per week over a span of five weeks and a single treatment duration of at least 30 min appear to have the most positive effects [15,17]. Although the antidepressive effects of massage therapy seem to be relatively well established, the basic mechanism of action remains unclear. However, evidence exists for various associated changes on either a biological or psychological explanatory level (see below). Depression is characterized by various symptoms. Thus, the question arises which single symptoms are alleviated by massage therapy? According to some papers [21,29,30] massage therapy is able to reduce depressed mood, state anxiety, perceived stress, somatic and mental fatigue, restlessness and muscular tension. The antidepressive effect seems to be more marked than the anxiolytic effect [15,17].

In the following, we are going to propose a hypothetical mechanism of touch-related antidepressive treatment based on modern interoception research. First, interoceptive disturbances in depression will be presented. Second, we will refer to human skin as a target organ for interoceptive treatments. Third, we will classify massage therapy as possibly one of the most ancient interoceptive treatments and will highlight its transdiagnostic treatment characteristics.

**Interoception and depression**

Interoception is defined as the sense of the physiological condition of the entire body [31,32]. It comprises the sensation, interpretation, and integration of signals arising from within the body [33]. Different facets of interoception have been proposed [34]: interoceptive accuracy (“objective accuracy in detecting internal bodily sensations”), interoceptive sensitivity (“self-perceived dispositional tendency to be internally self-focused and interoceptively cognisant”) and interoceptive awareness (“metacognitive awareness of interoceptive accuracy”). In psychiatric research, most of published work has focused on the study of interoceptive accuracy [35] by using the Schandry task. This heartbeat mental tracking task assesses the ability of a subject to accurately count the number of one’s heartbeats in a series of trials without taking the pulse [36]. The task is widespread since it is an easy to be used and non-invasive accuracy measure. To the best of our knowledge, other interoceptive modalities like gastric or rectum perception accuracy as well as assessment of interoceptive dimensions other than interoceptive accuracy (e.g. interoceptive sensitivity) have rarely been assessed so far in depression research, possibly due to their invasiveness and due to incongruencies in construct validity among available interoceptive self-report scales [35,37].

Interoception is increasingly considered as substantial for the understanding of psychopathological and psychosomatic processes. Several mental disorders have been associated with impaired interoceptive functioning [38–40]. It has been shown that severity of MDD is associated with disturbances in interoceptive accuracy (for a comprehensive review, see [41,42]). Thus, moderately depressed subjects exhibit the largest deficits in accurately perceiving their heartbeats [43–48]. These patients may be classified as poor heartbeat perceivers since they underestimate the number of their heartbeats in the heartbeat mental tracking task. However, cardiac interoceptive accuracy scores have been reported to normalize with increasing depression severity. It has been speculated that these “normalizing effects” may be confounded by intake of selective serotonin reuptake inhibitors or by comorbid anxiety disorder [43]. In summary, impairments in interoceptive functioning depend on depression severity with moderately depressed subjects exhibiting the largest deficits to perceive their heartbeats.

It has also been investigated whether single symptoms of depression are associated with interoceptive impairments. In a study with clinically depressed subjects, those with decision-making difficulties exhibited significantly worse heartbeat perception abilities than subjects without decision-making difficulties [45]. Furthermore, it has been shown that the intensity of positive affect positively correlates with cardiac interoceptive accuracy in MDD. Thus, poor heartbeat perceivers are experiencing reduced intensities of positive emotions [45]. These findings may imply that anhedonia is intimately linked to blunted heartbeat perception in depressed subjects. Finally, suicidality including suicidal ideation as well as planning and attempting suicide has been linked to a distorted interoceptive awareness [49,50].

It is currently unclear if interoceptive impairments are a cause or consequence of depressive disorders [33]. Besides, it is unclear why the perception of heartbeat activity is blunted in depression [45]. Despite increasing interest in depression-related interoceptive deficits [43–48], treatment approaches that explicitly target the interoceptive system of depressed subjects are scarce in clinical practice but currently under investigation, e.g. in the form of whole-body hyperthermia [51], Flotation-REST (Reduced Environmental Stimulation Therapy) sessions [52], or functional magnetic resonance imaging neurofeedback training [53,54].

**A plea for interoceptive treatments**

There is a need for the development of new treatment strategies that both target the interoceptive system and alleviate interoceptive impairments in a variety of psychiatric or psychosomatic patients [33]. Challenges in developing interoceptive treatments generally raise two substantial issues: a) Is there any way to counteract interoceptive deficits (e.g. impaired interoceptive accuracy)? b) Do interventions that influence interoception (e.g. by increasing interoceptive accuracy) result in changes of mental states? If there is scientific evidence to answer in the affirmative these two basic questions, the essential condition underlying interoceptive treatments may be met. Hence, we will first briefly discuss these topics in the following section. Then, we shall develop a novel hypothesis on the mechanisms of affective massage therapy in depression.

Various studies suggest that interoceptive accuracy can be modulated by therapeutic interventions and is thus not immutable. Both cardiac biofeedback training and exercise in body awareness (“body scan” meditation) have been shown to improve interoceptive accuracy in healthy adults [55–57]. However, interoceptive treatments will only be of clinical significance if changes in interoceptive performance imply significant clinical effects. Thus, Bornemann et al. [56] demonstrated that improvement of interoceptive accuracy through a body scan intervention over nine months is associated with an increase in emotional awareness by reducing alexithymia – an observation which appears significant since alexithymia and depression are closely linked [58]. Alexithymia predicts poor performance in heartbeat perception task [59] comparable to the influence of depression. According to Schaefer et al. [60] a heartbeat perception training significantly reduced symptom distress in participants with somatoform disorder. Against the background that higher somatic symptom severity is correlated with decreased cardiac interoceptive accuracy in somatoform disorder [61], the findings of Schaefer et al. seem to be of special importance. Somatic disturbances are also highly prevalent in depression [62]. Interoceptive impairments may be linked with affective and somatic symptoms of depression for several reasons [42]: First, evidence suggests morphological and functional abnormalities in interoceptive brain areas (e.g. insula, anterior cingulate cortex, orbitofrontal cortex) which have been associated with both depression severity and somatic symptom severity [42,63,64]. Second, vagal nerve stimulation has shown promising results in treatment-resistant depression [65] suggesting an interoceptive involvement [66]. The vagus nerve converges with interoceptive afferents that form interoceptive brain centers. Transcutaneous vagus nerve stimulation is capable to modulate interoceptive brain networks [33,66,67]. Thus, the antidepressant effects might be mediated by increasing interoceptive accuracy since vagal nerve stimulation has shown to increase spontaneous cardiac baroreflex sensitivity [67,68].
Arterial baroreceptors are “cardiac interoceptors” [68,69] and baroreceptor sensitivity has positively been correlated with cardiac interoceptive accuracy in a single report [68]. Hence, vagal stimulation probably impinges on the body-brain-axis by reducing signal-to-noise ratio in interoceptive processing [42]. In conclusion, preliminary evidence suggests that therapeutic modulation of interoceptive accuracy may result in alleviation of affective and somatic symptoms of depression.

Affective massage therapy and its hypothetical antidepressive mechanism

In the following, we are going to delineate the characteristics of those massage techniques which have been shown to elicit mental effects. There exist many different types of massage (e.g. deep tissue massage, hot stone massage, sports massage, shiatsu massage etc.) that focus on various parts of the body resulting into individual massage therapy outcomes (e.g. muscle relaxation in Swedish massage). Following Moyer [70], we prefer the term affective massage therapy which includes all types of massage therapies aiming to influence affective states rather than primarily loosing muscles or manipulating fascial tissues. It is important to note that affective massage therapy is not another new therapy type. Instead, the term affective massage therapy comprises various massage styles that induce psychophysical effects and share common characteristics: First, such massages operate within a context emphasizing the intention of the massage therapist to alleviate psychopathological symptoms or to enhance psychophysical well-being. Second, affective massage therapy predominantly makes use of massage techniques such as effleurage (i.e. soft stroking) having been shown to affect positively e.g. mood, anxiety or perceived stress. A major limitation of a wide range of publications on affective massage therapy is the lack of a concise description of the applied massage techniques. However, as we have shown in a clinically depressed population as well as in a mildly depressed community sample, long strokes and caress-like touch yielded clinically significant effect sizes regarding reductions in depression severity [21,71]. Effleurage is also used in the well-known Swedish massage tradition. These techniques closely resemble affective touch – a term coined by neurophysiologists defining gentle stroking conditions (e.g. with a brush) within an optimal velocity range between 1 and 10 cm/s that is associated with a response of specialized C fibers in the human skin (see below). Affective touch elicits a subjective sense of psychophysical well-being that has been correlated with activations in limbic cortical areas [72–74]. Recent evidence suggests that manual foot massage for 10 min not only resembles affective touch but elicits stronger activations than machine administered touch in cortical areas that have been linked with affective touch [74]. Therefore, following Occam’s razor principle, we shall operationalize affective touch by hand as a core element of affective massage therapy since affective touch is an established and widely accepted concept having gained remarkable scientific interest during the last decade.

The essential mechanisms behind antidepressive effects of affective massage therapy so far have remained unclear [17,18]. For example, it has been reasoned that massage elicits a decrease in stress response [75]. However, effects of massage on cortisol plasma/saliva levels are very small or even not significantly different from zero. Thus, it seems unlikely that decreases in cortisol levels could be seen as the basic mechanism of widely documented antidepressant, anxiolytic and analgiesic effects of affective massage therapy [76]. Other mechanism have been proposed to explain affective outcomes of massage therapy [17]: whereas the Touch Research Institute has always stressed the shift to parasympathetic activity [77], others have underlined influences on body chemistry (serotonin and endorphins), promotion of restorative sleep, interpersonal attention, or simple relaxation effects [12]. The release of oxytocin might play an important role [78]. Effects on the immune system have also been documented [79]. Recent research suggested that massage therapy may train interoceptive skills that elicit adaptive emotion regulation strategies [80] by improving somatic awareness in posttraumatic stress disorder [81].

Affective massage therapy directly stimulates the interoceptive nervous system by application of affective touch which arouses particular afferents in the non-glabrous skin that respond to social touch interactions and elicit a state of well-being [73]. Accumulating neuroanatomical evidence suggests that the non-glabrous mammalian skin contains numerous mechanosensitive receptors which give rise to subjectively perceived pleasantness in response to slow, rhythmic, and caress-like touch [73]. These unmyelinated C tactile (CT) afferents encode affective rather than discriminative features of touch [72]. CT afferents project to the insular cortex via the lamina I spinohalamic-cortical pathway that relays homeostatic information to the insula and other interoception-related brain regions [31,32]. It has been speculated that this homeostatic pathway forms the basis for the construction of affective states and self-awareness [31]. An abundance of research has shown that CT afferents are involved in the maintenance of psychophysical and social well-being [73,82–84]. Furthermore, optimal stimulation of CT afferents (stroking touch velocity ~3 cm/s) elicits positive affective states with activation of the zygomaticus major muscle [85]. Accordingly, the antedressant effects of affective massage therapy might be in part mediated by optimally activating the CT network through application of affective touch [71]. Following this concept, psychosomatic effects of affective touch possibly result in an enhancement of bodily self-awareness [86] and an activation of interoceptive regulation mechanisms [87,88] that presumably mitigate abnormal interoceptive representations in depression. In fact, a recent study has demonstrated that gentle touch increases interoceptive accuracy in healthy adults highlighting the skin as a gateway to modulate interoceptive accuracy [89]. At the neurophysiological level, the insula (or primary interoceptive cortex) might be a key structure to study the proposed interoceptive mechanism. Insula activity is significantly decreased in depressed subjects during a heartbeat perception task compared to healthy controls. Besides, depression severity is negatively correlated with insula activity [63]. Furthermore, it has been shown that CT fiber mediated touch elicits increased activity in the insula in healthy adults [90]. Despite lack of published work, it can be assumed that affective touch also elicits responses in the insular cortex of depressed subjects. Hence, affective massage therapy could mitigate the above mentioned abnormal interoceptive representations in the insula.

Considering impaired interoception in depression, CT afferents and their relation to the interoceptive nervous system could be the missing link for explaining mental effects of affective massage therapy. To our best knowledge, such an association has never been tested before in depressed subjects. Additionally, it has been suggested that effects of massage therapy are mediated by pressure receptors lying in and beneath the skin that, in turn, stimulate vagal activity [91]. The parasympathetic activation possibly complements massage therapy’s effects on interoception since the vagus nerve is part of the interoceptive nervous system [for review Ref. [42]]. As outlined above, transcutaneous vagal stimulation improves spontaneous cardiac baroreflex sensitivity [67] that has been associated with higher interoceptive accuracy [68]. In summary, affective touch is not only promoting positive affective responses, but also elicitng psychophysiological changes that are intimately associated with the interoceptive nervous system [92]. Thus, it appears plausible to assume that the human skin could be a particularly safe gateway to modulate interoceptive states.

Future research may examine the hypothetical mechanisms that have been proposed regarding mental effects of affective massage therapy. We recommend the use of manual massage rather than using machine touch since machine administered massage elicits weaker

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*The following search terms yielded no document match in PubMed: interocept* AND (massage OR touch) AND depress* (date: November 2018).*
cortical and oxytocin responses [74]. First, pilot studies may investigate the impact of affective massage therapy on interoceptive accuracy in healthy adults using the heartbeat tracking task [36]. In addition, randomized controlled trials including clinically depressed subjects would be worthwhile.

Affective massage therapy as a transdiagnostic intervention?

Interceptive disturbances do not exist exclusively in depression. Instead, impaired interoception is a transdiagnostic characteristic of several mental disorders such as panic and generalized anxiety disorder [93], eating disorder [94,95], substance use disorder [96], somatic symptom disorder [35], or autism spectrum disorder [97]. Furthermore, interceptive disturbances have been associated with an abundance of painful and nonpainful clinical conditions, e.g. increased/decreased appetite, itch, fatigue, myalgia, or headaches [33]. Accordingly, affective massage therapy has shown to be effective in the complementary management of disorders other than depression, e.g. generalized anxiety disorder [98], chronic pain conditions [99–101], or cancer-related fatigue [102]. Therefore, affective massage therapy may be classified as a transdiagnostic intervention that merits high-quality research in psychiatry and psychosomatic medicine. Against the background of current neuroscientific knowledge and considering the interoceptive nervous system as well as CTs of afferents in the human skin [31,32,66,73], studies investigating effects of affective massage therapy may be built upon a scientifically well-established theoretical framework that incorporates interoception research.

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Declarations of interest

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