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Massage therapy research review

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A B S T R A C T

Moderate pressure massage has contributed to many positive effects including increased weight gain in preterm infants, reduced pain in different syndromes including fibromyalgia and rheumatoid arthritis, enhanced attentiveness, reduced depression and enhanced immune function (increased natural killer cells and natural killer cell activity).Surprisingly, these recent studies have not been reviewed, highlighting the need for the current review. When moderate and light pressure massage have been compared in laboratory studies, moderate pressure massage reduced depression, anxiety and heart rate, and it altered EEG patterns, as in a relaxation response. Moderate pressure massage has also led to increased vagal activity and decreased cortisol levels. Functional magnetic resonance imaging data have suggested that moderate pressure massage was represented in several brain regions including the amygdala, the hypothalamus and the anterior cingulate cortex, all areas involved in stress and emotion regulation. Further research is needed to identify underlying neurophysiological and biochemical mechanisms associated with moderate pressure massage.

Massage therapy is one of the most effective and widely used alternative therapies. Although most massage therapy sessions are for pain, recent research suggests that it is effective for other conditions including growth of premature infants, ADHD, depression, and immune conditions, most especially cancer (see Field, Diego, & Hernandez-Reif, 2007 for a review) [1]. In this paper recent data are reviewed on massage therapy effects and potential underlying mechanisms for those effects.

Although this review does not cover all conditions that have been positively affected by massage, it is focused on some specific conditions for the following reasons: 1)moderate versus light pressure data are reviewed inasmuch as moderate pressure is critical for achieving the positive effects of massage, findings that are important to communicate to therapists and clients alike; 2) preterm infant massage data are reviewed because of preterm infants' need for supplemental stimulation such as massage therapy for optimal growth and development and the importance of conveying that to the medical community so that it can be adopted into practice; 3)pain syndromes are the most common presenting complaints to many complementary and alternative therapists such as massage therapists and to worker's compensation; 4) attentiveness is critical for optimal school and job performance; 5) depression has negative effects on the immune system; and 6)the reduction of cortisol by massage therapy leads to increased natural killer cells and natural killer cell activity. Natural killer cells, in turn, ward off viral, bacterial and cancer cells, and in that way enhance immune function and reduce illness and disease.

1. Preterm infants

Our first massage therapy study focused on weight gain in preterm infants [2]. Since then, preterm infant massage has been noted to increase weight gain in studies from neonatal intensive care units in many parts of the world (see Field, Diego, & Hernandez-Reif, 2010 for a review) [3]. In most of these studies our 15-min protocol of moderate pressure massage (moving the skin) was used twice per day for a one-week period. After we documented preterm infant weight gain following massage in several studies, we reported data showing increased vagal activity and gastric motility, which could be leading to more efficient food absorption and increased weight gain [4,5].

In another study, we noted higher levels of insulin and IGF-1 growth factor when we compared a massage group who received three, 15-min massages per day for five days to a control group who received standard nursery care without massage therapy [6].The massage group had greater increases in: 1) weight gain; 2) serum levels of insulin; and 3) serum levels of IGF-1. Weight gain was

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correlated with insulin and IGF-1 levels. Path analyses suggested that increased vagal activity was associated with increased gastric motility, which, in turn, was related to greater weight gain, and increased IGF-1 was also related to greater weight gain. The increased vagal activity during the massage contributed to 49% of the variance in the increased gastric activity. And, the increased vagal activity during the massage explained 62% of the variance in the increase in insulin levels. These findings suggested two potential pathways by which massage can increase weight gain: 1) insulin release via the celiac branch of the vagus; and 2) increased gastric activity via the gastric branch of the vagus [7].

Increased temperature is another potential underlying mechanism for the massage therapy effects on weight gain inasmuch as lower temperatures are associated with energy expenditure that could result in weight loss. Temperature was assessed in preterm neonates randomly assigned to a control or massage therapy group [8]. Temperature increased more in the preterm neonates receiving massage, even though the incubator portholes were open during the 15-min massage therapy sessions (which would be expected to lower their temperature). This likely resulted from the heat-producing effect of rubbing the skin.

Another group explored reduced energy expenditure as a potential underlying mechanism in preterm neonates receiving massage [9]. This research team used the same massage therapy protocol as the one used in our preterm infant studies. Their metabolic measurements by direct calorimetry suggested that energy expenditure was significantly lower in the preterm infants after a five-day massage therapy period than after a period without massage. This decreased energy expenditure may be in part responsible for the increased weight gain associated with massage therapy.

Moderate pressure was a critical factor for the weight gain effect. This was documented in a study in which we directly compared moderate (moving the skin) versus light pressure (light stroking) massage [10]. In that study, the moderate versus light pressure massage group gained more weight per day, and, as suggested, during behavior observations that followed the massage they showed significantly less: 1) active sleep; 2) fussing; 3) crying; 4) movement; and 5) stress behavior (hiccupping). They also had lower heart rate and greater vagal activity. All of these changes suggested lower arousal, which, in turn, could explain the enhanced immune function noted in preterm neonates following massage in a study on delayed-onset sepsis [11]. In that study, mothers massaged their infants on the face and limbs as well as passively exercised their upper and lower limbs four times a day. The incidence of delayed-onset sepsis was significantly lower in the massage group who also had a shorter hospital stay (by 7 days), which likely resulted from the lower incidence of sepsis. A potential pathway for the moderate pressure massage effects may be increased vagal activity, decreased cortisol, enhanced immune function and reduced sepsis. Inflated pro-inflammatory cytokines such as IL-1, IL-6 and TNF-alpha should also be measured for their contribution to sepsis and their potential reduction by moderate pressure massage.

Several follow-up studies across infancy have revealed significant developmental benefits for massaged premies [12]. Despite these positive effects of massage therapy on preterm infants, the incidence of preterm delivery would ideally be decreased. Inasmuch as there is a disproportionate incidence of preterm infants born to depressed women, massage was used as a prenatal intervention for those women in several studies. In at least 4 studies, massaging depressed pregnant women resulted in better neonatal outcomes (less prematurity and low birthweight) [13–16]. These effects likely derived from decreased levels of cortisol and norepinephrine resulting in lower intrauterine artery resistance. Inasmuch as the uterine artery carries oxygen and nutrients to the fetus, the constriction of the artery could lead to prematurity and lower birthweight [1].

Full-term infants also benefit from massage. In one study, for example, full-term newborns who received moderate versus light pressure massage from their mothers gained more weight and had better development over the first month of life. [17] During the first several months, infants who are massaged have less irritability and sleep disturbance which are the most common complaints to pediatricians [1].

2. Pain syndromes

Massage has resulted in reduced pain in all the studies we have conducted on chronic pain conditions from lower back pain during pregnancy to labor pain, migraine headaches, premenstrual syndrome, chronic fatigue, fibromyalgia, carpal tunnel syndrome and rheumatoid arthritis [1]. In most of these studies the moderate pressure massage was focused on the painful area, such as the lower back, and the 20-min sessions were given twice per week for 5 weeks. In a recent review, the majority of the 25 studies that were covered employed a similar massage lasting 20–30 min and given twice-weekly over 5 weeks with assessments before and after the first and last session (at the end of the treatment period) [18]. These authors reported consistent single treatment reductions in salivary cortisol and heart rate and multiple treatment reduction in diastolic blood pressure (which has been recently replicated by Givi, 2013) [19]. Massage has also been effective for children and adolescents attending a chronic pediatric pain clinic [20]. After the therapy sessions, the children and adolescents reported significantly lower levels of pain, discomfort and depressed mood. In a study on postoperative pain management in adults, back massages resulted in decreased pain intensity as well as lower anxiety levels [21].

Arthritis patients have also experienced less pain following massage. For example, individuals with hand arthritis had less pain and greater grip strength following massage therapy [22] and even less pain when applying a topical analgesic following the massages [23]. Similar data have been noted for carpal tunnel syndrome [24], which were recently replicated by two studies using the same massage and measurement protocol [25,26]. Moderate versus light pressure massage has also been effective for rheumatoid arthritis in the upper limbs [27]. In that study entitled “Rheumatoid arthritis in upper limbs benefits from moderate pressure massage therapy” the adults with arthritis were randomly assigned to moderate or light pressure massage therapy groups. The participants were massaged on the wrists, arms and shoulders once a week for one month and they were also taught the massage and asked to massage themselves once a day. The moderate versus the light pressure massage therapy group had less pain and greater grip strength following the first and last massage sessions. By the end of the one – month massage period the moderate pressure versus the light pressure group had less pain, greater grip strength and greater range of motion in their wrists, elbows, and shoulders. Several studies on shoulder and/or neck pain, including one from our research institute, have yielded similar results [28–31]. A meta-analysis on 12 studies on neck and shoulder pain showed immediate and short-term effects for massage therapy [32]. And headaches associated with neck pain have also been reduced by massage therapy, although spinal mobilization techniques were more effective in that study [33].

Research on the lower limbs has focused on the knee. Massage outcomes have been positive for osteoarthritis of the knee [34] in which a dose response curve was noted with a plateau at 60 min per week. Pain has also been relieved by massage therapy following arthroscopic surgery for the knee in this case on a 20 min/week schedule [35].

The positive effects of the massage therapy in some of these studies have been equivalent to active therapies including physical therapy. In a review of 9 systematic studies on the use of massage therapy for low back pain, for example, massage was more effective than placebo [36]. However, conflicting findings were noted for studies that compared massage with other manual therapies such as mobilization and acupuncture.

Massage has also been effective for both acute pain and mood in a study on cancer patients [37]. In that research, adults with advanced cancer and moderate-to-severe pain who were enrolled in hospice received six 30-min massages or simple-touch sessions for two weeks. Massage was more effective than simple-touch for immediate pain relief and mood shifts. Similar data have been reported for breast cancer patients [38]. A review of 19 empirical studies and 8 review articles confirmed these data [39]. According to these authors, 73% of cancer patients use massage therapy in the U.S. Some large cancer centers in the U.S. have integrated massage therapy into their programs based on the positive effects of massage on cancer pain [40]. Other painful conditions have benefited from massage including burn wounds [41], post cardiac surgery pain [42–44], fibromyalgia [44,45], and Parkinsons [46]. And, in a study on pain management in hospital inpatients from medical, surgical and obstetrics units, significant reductions in pain were reported (50% reduction on visual analog scales) accompanied by less sleep disturbance [47].

Although most of the pain studies have been conducted on patients in hospitals or clinics, laboratory research has also been reported on the effects of massage on pain. For example, one group studied the effects of massage on mechanical pressure pain thresholds and perceived pain [48]. The participants were assigned to a moderate pressure massage group, a superficial touch group or a no-treatment control group. Exercises were then performed to induce delayed onset muscle soreness. The moderate pressure massage group experienced decreased pain (by 48%) during the exercises.

3. Potential underlying mechanisms for moderate pressure massage reducing pain

The mechanism that has been most frequently used to explain massage therapy effects on pain syndromes is called The Gate Control Theory [1]. According to that theory, pain is thought to stimulate shorter and less myelinated (insulated) nerve fibers so that the pain signal requires more time to reach the brain than pressure signals which are carried by nerve fibers that are more myelinated and longer and therefore able to transmit the pressure stimulus faster than the pain stimulus can be transmited. The pressure stimulus reaches the brain prior to the pain message and “closes the gate” to the pain stimulus. This metaphor has been used for the electrical and biochemical changes that are thought to occur following a pain stimulus. However, this theory has been controversial [49].

Another theory relates pain to deep sleep deprivation. In deep sleep, less substance P is released and therefore less pain occurs because substance P causes pain. We tested the “enhanced deep sleep leads to less substance P” theory in our study on patients with fibromyalgia [50]. Following a one -month period of massage therapy, more time was spent in deep sleep, and lower substance P levels were noted in saliva samples. Reputedly, lamina I of the superficial dorsal horn contains the main concentration of spinal substance P responsive neurons [51].

Still another theory is that with increasing serotonin levels pain is decreased inasmuch as serotonin is the body's natural anti-pain neurotransmitter [52]. Serotonin levels are increased by massage therapy and are also correlated with decreased cortisol and depression, which are also important effects of massage therapy. And, serotonin is also related to decreased substance P. Further research is needed to test these models. Basic problems for hands-on therapy research like massage are the ethical problem of randomly assigning individuals to a no-treatment control group when a treatment is known to be effective as well as the inability to double-blind the studies.

4. Attentiveness and EEG patterns

Increased attentiveness has been noted in a laboratory study by our group following 15-min chair massages [53].EEG patterns of heightened alertness/attentiveness occurred following the massage sessions including increased beta and theta waves and decreased delta waves. These EEG patterns were related to better performance after the massage on math computations including performing the calculations in less time and with greater accuracy immediately after the massages.

The massage effects on attentiveness might be mediated by increased vagal activity. The vagus nerve branch to the heart slows heart rate [54]. Increased vagal activity has been associated with enhanced attentiveness, and in several studies enhanced attentiveness has been associated with decreased heart rate [55]. The stimulation of pressure receptors by moderate versus light pressure massage is associated with decreased heart rate and EEG patterns that, in turn, are related to enhanced attentiveness [56]. Increased vagal activity may mediate the effects of moderate pressure stimulation on attentiveness. Enhanced attentiveness in children with autism and adolescents with ADHD following moderate pressure massage may also be mediated by increased vagal activity [1].

5. EEG and other correlates

Depressed individuals often have greater right than left frontal lobe EEG activity [57] Greater right frontal EEG activation is associated with negative emotions and with withdrawal or less approach behavior [57]. Chronically depressed individuals show this EEG pattern even when they are no longer showing behavioral symptoms [57].Thus, right frontal EEG has been noted as a physiological marker for chronic depression. Frontal EEG has shifted from right to left in depressed adolescents [58] and adults even after a short session of moderate pressure massage [59]. Other changes following massage therapy include increased vagal activity, that is typically low in depressed individuals [60].The flat facial expressions and vocal intonation contour noted in depressed individuals could be explained by low vagal activity given that the vagus nerve stimulates the face and voice muscles [54].

Cortisol levels that are often high in depression have decreased following moderate pressure massage [60] as have neurotransmitters associated with stress, i.e. norepinephrine levels [61]. And, serotonin (the body's natural antidepressant) and dopamine (an activating neurotransmitter) have increased following moderate pressure massage [52].

6. Immune function

Children with cancer have benefited from moderate pressure massage [62]. After four weekly massage sessions alternated with four weekly quiet-time control sessions, massage reduced heart rate and anxiety levels in the children, although immune function was only marginally improved in these children.

Natural killer cells and natural killer cell activity have increased following moderate pressure massage [1]. These data are promising given that natural killer cells are noted to ward- off viral cells, bacterial cells and cancer cells .Natural killer cell activity has

increased in preterm infants who received massage compared with sham therapy (light pressure massage control) [63]. Natural killer cells have also increased in children with HIV following massage [64]. Further, natural killer cells increased following a one-month period of moderate pressure massage for HIV- infected adolescents [65].CD4 cells (the cells that are killed by the HIV virus) also increased in the adolescents, suggesting an improved clinical condition. Natural killer cells and natural killer cell cytotoxicity (activity) also increased in our studies on women with breast cancer [66,67]. These women would also be expected to show clinical gains given that natural killer cells destroy cancer cells [68]. Stimulation of pressure receptors, as in moderate pressure massage, increases vagal activity, which reduces cortisol levels and thereby saves immune cells inasmuch as cortisol kills immune cells [69]. Other immune functions such as pro-inflammatory immune cells (cytokines) and shifts in immune balance are also involved. For example, in one study, massage therapy was given to young men after exercise-induced muscle damage [70]. Massage attenuated the production of inflammatory cytokines (tumor necrosis factor-a and interleukin-6). In a study on immune balance, an increase was noted in the Th1/Th2 ratio (a positive shift in immune balance) in breast cancer patients following 5 weeks of biweekly massages [71].In another study assessing healthy individuals, salivary chromogranin A increased following back massage, which, as the authors suggested, could lead to enhanced immune function given that chromogranin A is noted for its antibacterial and antifungal activity [72].

7. Moderate pressure appears to be necessary for these effects

Moderate pressure appears to be necessary for increased vagal activity and its effects [59,69]. That moderate pressure massage is more effective than light pressure massage suggests the involvement of pressure receptors. Animal studies indicate that stimulating pressure receptors activates the vagus nerve [73,74]. These data are consistent with our findings that lower heart rate and EEG patterns of lower arousal were associated with moderate versus light pressure massage [56].In this study, three different types of massage were assessed in a sample of adults who were randomly assigned to: (1) moderate pressure (moving the skin) massage, (2) light pressure (lightly stroking the skin) massage, or (3) vibratory stimulation (from a vibrating hand-held massage wand) [56]. Anxiety scores decreased for the 3 groups, but the moderate pressure massage group had the greatest decrease in anxiety, heart rate and EEG changes including increased delta and decreased alpha and beta activity, suggesting a relaxation response. The moderate pressure group also showed more positive affect and a shift toward left frontal EEG activation. The light pressure massage group, in contrast, had increased arousal, including increased heart rate and decreased delta and increased beta activity. The vibratory stimulation group also showed increased arousal, as indicated by increased heart rate and increased alpha and beta activity.

In another study we conducted on different pressure massages, adults were randomly assigned to a moderate pressure or a light pressure massage group, and EKGs were recorded [69]. Vagal activity increased for the moderate pressure massage group and decreased for the light pressure group. Another lab reported that following moderate pressure massage, oxytocin increased and ACTH (the precursor of the stress hormone cortisol) decreased [75]. For the massage group, the research team assessed 15 min of moderate pressure massage of the upper back. The control group rested quietly for 15 min. Comparisons of pre-post blood values suggested greater oxytocin levels and lower ACTH, nitric oxide and beta-endorphin levels in the moderate pressure massage group.

Researchers have also quantified the changes in muscle activity that occurred after different pressure massages. Compared with light pressure massage, moderate pressure massage produced a greater reduction in the stretch reflex [76]. As the author suggested, the fact that the stretch reflex is reduced by moderate pressure massage suggests that it may produce some of its beneficial effects by “reducing excitability in alpha motor neurons”. A reduction in the stretch reflex would be desirable because spinal hyperexcitability is associated with chronic pain syndromes [76].

8. Moderate pressure massage increases vagal activity and decreases cortisol

The model we have been exploring for the massage effects is that moderate pressure (as in stimulation of pressure receptors under the skin) enhances vagal activity which, in turn, reduces cortisol leading to many effects including reduced pain and increased immune function. Vagal activity consistently increases following moderate pressure massage [4,56]. This may have occurred via stimulation of pressure receptors, which ultimately signal the limbic system including hypothalamic structures involved in cortisol secretion.

Anatomical studies suggest that baroreceptors, and to a lesser extent, mechanoreceptors within and beneath the skin (i.e. Pacinian corpuscles) transmit signals to the vagus (to the nucleus ambiguous and the dorsal motor nucleus of the vagus) [77]. Research also suggests that electrical vagal stimulation reduces cortisol levels in depressed individuals [78]. Also, as already noted, we have shown that moderate pressure massage (but not light pressure massage) increased vagal activity in both infants and adults [69]. Data from many studies confirm that massage therapy decreases heart rate [56], lowers blood pressure [79–81],and reduces cortisol levels [82]. And data from an fMRI study showed that following moderate pressure massage cerebral blood flow increased in several brain regions involved in depression and stress regulation including the amygdala and the hypothalamus [83]. These fMRI data suggest that moderate pressure massage involves hypothalamic regulation of autonomic nervous system activity, cortisol secretion and limbic activity associated with emotion regulation. Another group that has used functional magnetic resonance imaging noted that moderate pressure massage was represented in the anterior cingulate cortex [84]. They assessed four different touch conditions including human touch with or without movement and a rubber glove with or without movement. The force and velocity were held constant across conditions. Human touch was rated as most pleasant, particularly when combined with movement. The fMRI results suggested that human touch with movement most strongly activated the anterior cingulate cortex. The authors suggested that these data were consistent with findings on other rewarding pleasant touch.

Increased vagal activity is associated with lower heart rate and blood pressure as well as decreased cortisol levels [54]. Inversely, decreased vagal activity has been associated with increased cortisol levels [85]. Others have noted an inhibitory effect of vagal activity on hypothalamic pituitary adrenal function [86]. The decreased norepinephrine and increased serotonin levels we have noted following massage might also be mediated by increased vagal activity [52,87]. Further research is needed on the interactive effects of these biochemical changes.

9. Summary

Moderate pressure massage has increased weight gain in preterm infants, reduced pain in different syndromes including fibromyalgia and rheumatoid arthritis, enhanced attentiveness, reduced

depression and improved immune function (increased natural killer cells and natural killer cell activity). When moderate and light pressure massage have been compared, moderate pressure massage reduced depression, anxiety and heart rate, altered EEG patterns and increased vagal activity, as in a relaxation response. Increased vagal activity has also been associated with decreased cortisol following massage. Functional magnetic resonance imaging data have suggested that moderate pressure massage was represented in several brain regions including the amygdala, the hypothalamus and the anterior cingulate cortex, all areas involved in stress and emotion regulation.

Further research is needed to identify underlying neurophysiological and biochemical mechanisms associated with moderate pressure massage. Unfortunately, several methodological challenges compromise this research including finding suitable control groups, e.g. controls for touching, inasmuch as light pressure massage can be aversive. Double blinding is also impossible. Further, replication studies are limited given the expense of biochemical and neurophysiological measures and the limited research funding for alternative therapy studies once their positive effects have been documented. Thus, the need for further massage therapy research and studies on similar therapies is highlighted by this literature review.

Conflict of interest statement

None declared.

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