【Original Article】

The Effects of Massage Therapy on the Immune, Hematological and Psychological State of Adult Subjects

成人被験者に対するマッサージの免疫学的，血液学的，心理学的効果

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[ABSTRACT]

Objectives: To determine the effects of massage therapy on the immune and psychological state, and serum lipids levels.

Design: A non controlled trial with 32 subjects.

Setting: Kyoto Prefectural School for the Blind and Kyoto Prefectural University of Medicine.

Subjects: 32 adults aged from 18 to 56 years (10 males; 22 females).

Interventions: One 25-min whole body massage.

Outcome Measures: Changes in peripheral blood levels of red blood cells (RBC), hematocrit (Ht), white blood cells (WBC), lymphocytes, neutrophils, CD4+ lymphocytes, CD8+ lymphocytes, CD4+/CD8+ ratio, CD16+ lymphocytes, serum interferon-γ (IFN-γ), serum interleukin 6 (IL6), serum total cholesterol (T-CHO), low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c); saliva secretory IgA (s-IgA); State-Trait Anxiety Inventory (STAI).

Results: Psychological measures; Both state and trait anxiety scores decreased significantly (p<0.001). Serum lipids; Significant hemodilution and significantly decreased levels of serum T-CHO, LDLc and HDLc (p<0.001) were observed. Immune measures; Significant decreases of neutrophils (p<0.05) and CD16-positive cell counts (p<0.01) were recognized.

Conclusions: It was suggested from our result in the present study that massage therapy is an effective relaxation/stress management technique which could reduce anxiety and modulate immune function.

[Key words]

massage therapy, relaxation, immune system, anxiety, cholesterol

1. INTRODUCTION

Massage therapy has a long history and is one of the oldest forms of medical treatment in the world. It was first described in China in the second century B.C. and soon after in India and Egypt. Ever since, massage therapy has been used for various medical conditions¹. However, after the pharmaceutical revolution of the 1940s, massage therapy was forgotten and ignored in mainstream medicine.

With the recent boom in complementary and alternative medicine (CAM), massage therapy is attracting attention and becoming popular again. Generally, massage therapy is considered to improve circulation, facilitate the elimination of waste, reduce swelling, and soothe the function of the peripheral and central nervous systems.

One of the most common application of the massage therapy is reducing pain such as lumbago and headache², but use of massage for relaxation and reducing levels of anxiety is also getting popular. For example, massage therapy has been reported to reduce levels of anxiety and stress hormones and improve the clinical course in children under various medical conditions³. Regarding the psychiatric effects of massage ther-
apy, reduction in anxiety and hostility, as well as diminished depression, have been documented\(^4\). There is a letter about immunological effects of one time 1hr massage therapy on 9 healthy female medical students and they found increase in total WBC counts and increase in NK cell activity after the massage\(^5\). In addition, there have been three reports on the change in the immune functions of HIV-positive patients caused by massage\(^6\)–\(^8\).

In recent years, stress-related illnesses have severely impacted on the modern society and establishment of the effective stress management programs is an urgent and crucial public concern. A variety of psychological interventions employed for stress management and massage therapy could be of use as relaxation techniques for managing stress, modulating immune system and promoting health. To assess this possibility, the effect of massage psychological relaxation and on immune and hematological measures was examined in normal subjects in the present study.

2. MATERIALS AND METHODS

2.1 Subjects

This study was performed between August 22 and 29, 2002. We recruited 37 employees of the Kyoto Prefectural High School for the Blind and 9 students of the Kyoto Central School of Nursing as volunteers for our study. This study was conducted after obtaining approval from the Ethics Committee of Kyoto Prefectural University of Medicine. All the subjects were given the detailed explanations on the project and signature of informed consent form was obtained from them prior to participating. A questionnaire regarding oral medication and chronic disease was distributed. Thirty-seven subjects were on no medication, while 4 subjects took some.

2.2 Inclusion and exclusion criteria for subjects

Forty six adults aged from 18 to 62 years old were participated in the present study. Four subjects taking anti-hypertensive drugs and 1 subject taking an anti-cholesterol medicine were excluded from our statistical analysis because those drugs might have some effect on the result of the present study. Although one subject taking an iron supplement, one vitamin compounds, one helenien and one dipyridamole, these were not exclude from the study, since these medicines were not considered to affect the results. Nine smokers were also excluded from the analysis. As a consequence, thirty two patients were included in the statistical analysis of the present study (Table 1).

2.3 Procedure

First, immediately after subjects filled out the State-Trait Anxiety Inventory (STAI) form, blood was drawn and saliva was collected. Then, subjects received a 25-min massage therapy. After the massage, they filled out another STAI form. Immediately after they filled out the STAI form, blood was drawn and saliva was collected again.

2.4 Massage procedure

Massage therapy was performed by six skilled massage instructors of Kyoto Prefectural High School for the Blind. Massage therapy was delivered in a quiet therapy room in the Kyoto prefectural High School for Blind. The massage technique was based on Amma, a method of Chinese origin. Massage was performed on the whole body through a shirt from head and neck, shoulder, back and hip, to upper limb and lower limb for approximately 25 min in a lateral position on the massage bed. Techniques applied were effleurage, kneading with whole hands or kneading with thumb along muscle. Pressure applied by the massage was a level which subjects feel comfortable.

2.5 Method of Immune Measurements

Blood cell counts including numbers and proportions of leucocytes and serum lipid concentrations were examined at the Central Laboratory Unit of Kyoto Prefectural University of Medicine. Two milliliters of the heparinized blood samples was used to determine the levels of various lymphocyte subsets. Mononuclear cells were isolated by Ficoll-Paque\(^\text{TM}\) PLUS (Amersham Biosciences AB, Sweden) gradient centrifugation. Lymphocyte subsets were identified by FACS analysis (FACS Caliber, Becton, Dickinson and Company, Franklin Lakes, NJ) using FITC-CD16, PE-CD8 and FITC-CD4 antibodies (Becton, Dickinson and Company).

Serum samples were stored at −80°C until determination of interferon-\(\gamma\) (IFN-\(\gamma\)) and serum interleukin 6 (IL6) concentrations with ELISA kits (Pierce Biotechnology, Rockford, IL).

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<th>Table 1 Subjects characteristics</th>
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<tr>
<td>Number</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Age range (Years)</td>
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<td>Mean Age (Years)</td>
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Simultaneously, 0.5 ml of serum aliquot was sent to the Central Laboratory Unit of Kyoto Prefectural University of Medicine to examine serum total cholesterol (T-CHO), low-density lipoprotein cholesterol (LDL-c), and high-density lipoprotein cholesterol (HDL-c) levels.

2.6 Secretory immunoglobulin A (S-IgA)
Saliva samples were collected before and after the massage using Saliva collection test tubes (Salivette®, Sarstedt, Nümbrecht, Germany). The saliva was stored at –80°C in a freezer until S-IgA concentration was assayed using EIA s-IgA test (Medical & Biological Laboratories CO., LTD, Nagoya, Japan) following the kit’s instructions.

2.7 Psychological measure
STAI(9) was filled out as a psychological measure by the subjects immediately before and after the massage.

2.8 Statistical analysis
For the analysis of the results of psychological measure and blood examinations between pre- and post-session, paired t-test was used. Spearman’s rank correlation coefficient test was employed to analyze correlations between the initial levels of anxiety and the decreasing extent in STAI test.

3. RESULTS
3.1 Psychological response to treatment
Psychological responses to treatment were assessed as the change in anxiety using STAI. Both state anxiety and trait anxiety scores were significantly reduced after the massage compared with the baseline obtained before the massage. Notably, the mean state anxiety score dropped markedly from 39.59 to 29.03 (p<0.001; Table 2). The positive correlation of the initial STAI score with the delta STAI score (score obtained by subtraction of the score before session from that after it) was found (correlation coefficient=0.635, p<0.001).

3.2 Effects on plasma volume and serum lipids
In regard to serum lipids, T-CHO, LDL-c and HDL-c levels were found to be significantly decreased (p<0.001; Table 3). However, hematocrit (Hct) and red blood cell (RBC) counts were significantly decreased following massage therapy (p<0.001; Table 3), which suggests the hemodilution by massage therapy. Therefore, the serum T-CHO, LDL, and HDL levels were calibrated with Hct, and the decrease in serum T-CHO, HDL, and LDL levels were still statistically significant (p<0.001, 0.001, and p=0.01, respectively; Table 4). There was no significant difference in LDL to HDL ratio before and after massage (p=0.37; Table 4).

3.3 Effect on immune functions
The numbers of total leukocytes, neutrophils, and CD16-positive cells were found to be significantly reduced after the massage (p<0.001, 0.001, and =0.001, respectively; Table 5). After calibration of the cell count with Hct, the reduction in numbers of neutrophils and CD16-positive cells was still significant (p=0.01 and <0.01, Table 6), but total leucocyte and lym-

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<th>Table 2</th>
<th>Psychological changes with STAI</th>
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<tr>
<td></td>
<td>pre-test</td>
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<tr>
<td></td>
<td>mean</td>
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<tr>
<td>State-anxiety</td>
<td>39.59</td>
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<td>Trait-anxiety</td>
<td>45.12</td>
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n=32

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<th>Table 3</th>
<th>Blood cholesterol levels, RBC and Hct</th>
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<tr>
<td></td>
<td>pre-test</td>
</tr>
<tr>
<td></td>
<td>mean</td>
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<tr>
<td>T-CHO (mg/ml)</td>
<td>185.75</td>
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<tr>
<td>HDL (mg/ml)</td>
<td>58.84</td>
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<tr>
<td>LDL (mg/ml)</td>
<td>108.59</td>
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<tr>
<td>RBC (cells/μl)</td>
<td>4.44E+06</td>
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<tr>
<td>HCT (%)</td>
<td>40.16</td>
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n=32
The concentration of IFN-γ was below the detectable limit (10 pg/ml) in all samples. No significant changes were found in concentrations of serum IL6 and saliva s-IgA when values obtained before the massage were compared with those after the massage.

### 4. DISCUSSION

It was found in the present study that massage was effective at inducing relaxation in terms of decreasing anxiety levels, and these results were coincident with that of Field et al.\(^\text{10}\). Both trait and state anxiety scores were significantly reduced, and the latter was more than the former, which is reasonable because the “state anxiety” score represents a temporary condition that changes every moment, while the “trait anxiety” score represents more a general and long-standing quality of anxiety.

According to a former report\(^\text{11}\), the mean STAI score in normal adult subjects was state anxiety=36.3±8.98 and trait anxiety=38.8±9.68. Initial stress levels on STAI in our study were found to be state anxiety=39.59 and trait anxiety=45.12. These values were relatively higher than those for normal adults, but lower than those of psychosomatic and neurotic patients. This relatively high initial level could be due to the fact that many teachers participated in our study and teaching is generally considered to be a highly stressful occupation\(^\text{12}\).

In addition, because subjects with high initial anxiety levels tended to have more decreased anxiety scores after the massage therapy in our study, massage might be useful for reducing anxiety in patients with high anxiety levels such as psychoso-
matic and neurotic patients. It is rather unusual that trait anxiety was also reduced in our study which is thought to be due to the great change in state anxiety and partly due to social desirability bias.

In the present study, a significant decrease in Hct and RBC counts was observed, which may result from increased blood plasma volume, in other words, hemodilution, because stress-induced activation of the sympathetic nervous system causes an elevation of blood pressure and decreased blood plasma volume, in other words, hemoconcentration\textsuperscript{13}, and furthermore, the possibility of sudden decrease in the number of erythrocytes is very low.

Although we did not examine blood pressure, it is possible that blood pressure drops following massage as Meek and Hadfield reported\textsuperscript{14,15}. Therefore, one possible cause of the hemodilution would be due to lowered blood pressure by a down-regulation of the sympathetic nervous system and relative up-regulation of the parasympathetic nervous system following relaxation. Another possible cause of the hemodilution would be an increased lymphatic flow with shift of fluid from interstitial tissues to intravascular space.

Acute psychological stress is known to cause elevations of serum total cholesterol and its fractions\textsuperscript{13}. The blockade of the β1 receptor by a specific antagonist is known to attenuate stress-induced hypercholesterolemia in rats\textsuperscript{16}.

In the present study, after calibration of cholesterol concentration for hemodilution, a significant decrease in serum cholesterol following massage therapy was recognized, which suggests that relaxation with massage influences lipid metabolism and clearance, possibly through the down-regulation of the sympathetic nervous system and decreased levels of serum cholesterol. Furthermore, any changes were observed in LDL to HDL ratio.

In regard to immune measures, even after arithmetic correction with Hct, we observed a significant reduction in numbers of neutrophils and CD16-positive lymphocytes representing the natural killer (NK) cells were observed.

Granulocyte and lymphocyte subsets including NK cells have been reported to increase with sympathetic stimulation\textsuperscript{17} and the roles of the sympathetic and parasympathetic nervous systems in controlling the immune system are considered to be very important.

The hypothalamic-pituitary adrenal axis is also known to be important for mind-immune interaction. Positive correlations between plasma cortisol levels and neutrophil numbers are known\textsuperscript{18}. Because massage therapy is reported to decrease cortisol in 24-hour urine collections\textsuperscript{2}, the decreased neutrophil counts after massage therapy are probably a result of a relaxation-induced down-regulation of the sympathetic nervous system and reduced stress hormone levels.

One time 1 hr massage therapy on 9 healthy female medical students significantly increase total WBC counts and NK cell activity after the massage\textsuperscript{5}. Furthermore, it was reported in the case of HIV-positive patients that twenty 45-min massages in one month or twice a week for 12 weeks significantly increased NK cell numbers and cytotoxicity\textsuperscript{6,19}. The results in the present study were different from those, this difference may due to the short term effect of massage in the present study, while the long-term effects in their studies. Another reason is that we used CD16+ cells to represent NK cells, while they used CD56+ cells. CD16 and CD56 are both known to be expressed on NK cells and used NK cell surface marker; but respective antibodies detect slightly different populations\textsuperscript{20}.

In addition, other studies have reported that stress increases the proportion of NK cells\textsuperscript{21,22}. The decrease in NK cell counts after massage suggests that massage therapy may influence immune system, although it was not necessarily confirmed that massage activated immune system.

5. CONCLUSION

It was found in the present study that a 25-min massage was a 25 min of massage therapy is capable of inducing psychological relaxation in terms of reducing anxiety. Massage therapy also modulates immune function, induces hemodilution and decreases serum cholesterol. These suggest the possible usefulness of massage therapy as a stress management technique and health promotion in modern society.

ACKNOWLEDGEMENTS

The authors would like to thank the massage instructors of the Kyoto Prefectural High School for the Blind for performing the massage, and employees of Kyoto Prefectural High School for the Blind and students of the Kyoto Central School of Nursing for volunteering for the present study. We also acknowledge the help of Dr. Naohisa Fujita and staff of the Central Laboratory Unit of Kyoto Prefectural University of Medicine with hematological measurements.
REFERENCES

要  旨

成人被験者に対するマッサージの免疫学的、血液学的、心理学的効果

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2京都府立医科大学大学院医学研究科精神機能病態学
3立命館大学大学院医学研究科応用人間科学研究科
4有限会社健康館マッサージ鍼灸院

目的：マッサージの免疫学的、心理学的及び血清脂質に及ぼす影響を検討する。

デザイン：32名に対する被験者内比較試験

場所：京都府立盲学校及び京都府立医科大学

方法：18歳から56歳までの32人の成人（男性10人、女性22人）に25分間の全身のマッサージをおこない、白血球数、白血球分類、血清脂質、唾液分泌型IgA、STAI不安尺度(State-Trait Anxiety Inventory)などにつき検討した。

結果：心理学的指標；状態不安、特性不安、ともに有意に減少した。血清脂質；統計学的に有意な血液希釈が認められ、血清T-CHO HDL-c, LDL-cともに有意減少した(p<0.001)。免疫学的指標；統計学的に有意な好中球の減少(p<0.05)とCD16陽性細胞の減少(p<0.01)が認められた。

結論：以上により、マッサージ療法は不安を軽減し、免疫力および血清脂質濃度に影響を与えることが示唆された。

キーワード：マッサージ、リラクゼーション、免疫、不安、コレステロール