



# Fibromyalgia Pain and Substance P Decrease and Sleep Improves After Massage Therapy

Tiffany Field, Miguel Diego, Christy Cullen, Maria Hernandez-Reif, William Sunshine, Steven Douglas

Massage therapy has been observed to be helpful in some patients with fibromyalgia. This study was designed to examine the effects of massage therapy versus relaxation therapy on sleep, substance P, and pain in fibromyalgia patients. Twenty-four adult fibromyalgia patients were assigned randomly to a massage therapy or relaxation therapy group. They received 30-minute treatments twice weekly for 5 weeks. Both groups showed a decrease in anxiety and depressed mood immediately after the first and last therapy sessions. However, across the course of the study, only the massage therapy group reported an increase in the number of sleep hours and a decrease in their sleep movements. In addition, substance P levels decreased, and the patients' physicians assigned lower disease and pain ratings and rated fewer tender points in the massage therapy group. (*J Clin Rheumatol* 2002;8:72-76)

Key words: Fibromyalgia, Substance P, Massage therapy

Fibromyalgia syndrome (FM) is one of the most common conditions in rheumatology practice (1), affecting approximately 3 to 6 million individuals (mostly women) in the United States (2). The syndrome is defined as widespread chronic musculoskeletal pain of unknown cause and multiple tender points (3). Characteristically, the symptoms include generalized pain, myalgia, arthritis, nonrestorative sleep, irritable bowel, temporomandibular dysfunction, anxiety, depression, headache, and neuropsychiatric complaints (4-6). In addition, substance P levels are significantly elevated in this patient population (7,8). Several mechanisms have been explored, including that peripheral

pain mechanisms are activated in FM patients (7,9). An alternative mechanism involves abnormal microcirculation, calcium homeostasis, and microtrauma to muscle tissue (10). Others believe the origin of FM is in the central nervous system, namely disturbances in the serotonin pathway (7,11-13) leading to an  $\alpha$  sleep disturbance in stage 4 non-rapid eye movement sleep (7,11,12), lower pain thresholds and elevated substance P levels, and lower levels of somatostatin affecting muscle homeostasis, mass, and function (5,13).

Exercise, stretching, and body mechanics training have been used to increase activity in FM patients (14). Antidepressants have been use-

ful for increasing serotonin levels and in turn reducing FM symptoms (13). Nonmedical treatments such as relaxation therapy (15), cardiovascular fitness training (16), chiropractic management (17), electromyography biofeedback training (18), acupuncture (19), and even cryotherapy (whole-body cold therapy) (20) and mudpack treatment (21) have also proven promising.

We studied the effects of massage therapy on the reduction of pain, stiffness, fatigue, and sleeping difficulties in patients with fibromyalgia (22). In the previous study, 30 adult FM patients were assigned randomly to a massage therapy group, a transcutaneous electrical stimulation group, or a no-current transcutaneous electrical stimulation group for 30-minute treatment sessions twice weekly for 5 weeks. The massage therapy participants reported lower anxiety and depression, and their cortisol levels were lower immediately after the therapy

Touch Research Institutes (TF, MD, CC, MH-R, WS), University of Miami School of Medicine, Miami, Florida; Children's Hospital of Philadelphia (SD), Philadelphia, Pennsylvania.

Supported by National Institutes of Mental Health Senior Research Scientist Award MH00331 to Tiffany Field and a grant from Johnson & Johnson to the Touch Research Institutes.

Address correspondence to: Tiffany Field, PhD, Touch Research Institutes, P.O. Box 016820, Miami, FL 33101. E-mail: tfield@med.miami.edu  
Copyright © 2002 by Lippincott Williams & Wilkins, Inc.

sessions on the first and last day of the study. The transcutaneous electrical stimulation group showed similar changes after the therapy sessions on the first and last day of the study. By the end of the study, the massage therapy group had improved on the dolorimeter measure of pain. At that time, they also reported less pain, stiffness, fatigue, and fewer nights of difficult sleeping. These findings may relate to increased serotonin levels, because increased serotonin levels have been noted in other conditions after massage therapy (23). Low serotonin levels may contribute to the nonrestorative sleep, mood alteration, and increased pain sensitivity noted in FM patients (24). The adult findings were consistent with those reported by Yunus and Masi (25) on adolescents with fibromyalgia.

The purpose of this study was to explore the potential underlying mechanisms for the massage therapy effects reported in our earlier study (22). Massage therapy was expected to increase restorative

*...all participants continued their standard medical care.*

sleep, decrease substance P levels, and reduce pain.

## PATIENTS AND METHODS

### Participants

Twenty adult patients were recruited from a local university and bookstore discussion group on fibromyalgia and were randomly assigned to a massage therapy or relaxation therapy group. The university and bookstore samples were evenly distributed between the massage and relaxation therapy groups.

They averaged 9.2 years in treatment, 50.9 years of age, were of middle socioeconomic status ( $M = 2.2$  based on the Hollingshead Index), and were 85% white and

*...were recruited from a local university and bookstore discussion group on fibromyalgia...*

15% Hispanic. The two groups did not differ based on age, socioeconomic status, or ethnicity.

### Procedure

Before random assignment, a rheumatologist confirmed the diagnosis of fibromyalgia in the participants according to the criteria established by the American College of Rheumatology in 1990 (3). During the study period, all participants continued their standard medical care.

### Massage Therapy

Participants received a massage twice weekly for 5 weeks by a volunteer professional massage therapist. The massage, which was a combination of several types of massage including Swedish massage and Shiatsu, consisted of moderate pressure stroking of the head, neck, shoulders, back, arms, hands, legs, and feet for 30 minutes. The massage began with lengthening and stretching of the neck and spine with the hands positioned under the head and neck, followed by stroking the forehead and face. Pressure was applied to the tender points, and the shoulders were gently depressed. The arms and legs were stretched, and the arms were lifted and moved in a circular motion as in a Trager massage. Finger pressure was applied to the palms of the hands and the soles of the feet, with extra pressure given to

the tender points. Stroking was then continued from the top to the bottom of the limbs. Medium pressure squeezing was applied to the upper shoulder and neck area, and light, brisk rubbing movements were performed along the spine. The massage was concluded in each position with gentle rocking and more stroking from head to toe.

### Progressive Muscle Relaxation Therapy

A relaxation group was assessed to control for potential placebo effects or improvement related to the increased attention given to the massage therapy group participants. The relaxation therapy group was given instructions on how to conduct progressive muscle relaxation sessions for 30 minutes while laying quietly on the massage table, including tensing and relaxing large muscle groups starting with the head, neck, shoulders, back, arms, hands, legs, and feet. The therapist conducted these sessions twice weekly for 5 weeks with the participants.

### Assessments of Immediate Effects (Before and After Treatment Sessions on the First and Last Days)

The questionnaires and assessments were given before and after sessions on the first and last days of the study to measure the effects of the therapy in the following order.

*...a combination of several types of massage...*

The State Trait Anxiety Inventory (26) is an anxiety scale consisting of 20 items concerning how the participant feels at that moment in terms of severity from 1, not at all, to 4, very much so. Typical items include

"I feel nervous" and "I feel calm." The State Trait Anxiety Inventory has adequate concurrent validity and internal consistency ( $r = .83$ ). The Profile of Mood States (27) is a 5-point adjective rating scale on how well an adjective describes the participants' feelings, including helpless or gloomy feelings, depression, and anxiety. The scale has adequate internal consistency ( $r = .95$ ) and is an adequate measure of intervention effectiveness (28).

#### Assessments of Longer-Term Effects (Before Treatment Sessions on the First and Last Days)

The after assessments were given before treatment on the first and last days of the study. The Center for Epidemiological Studies Depression Scale (29) is a 20-item questionnaire that measures depressive symptoms over the past week on a 4-point scale. The responses are rated on frequency (rarely to most of the time), and characteristic items include "I felt depressed," "I had crying spells," and "I did not feel like eating, my appetite was poor." This scale has a high internal consistency ( $\alpha = 0.86$ ) and test-retest reliability, and validity has been established by cor-

relation with other self-report measures and by clinical ratings of depression (30,31). Studies have shown that a cutoff score of 16 or more can differentiate clinically depressed from nondepressed subjects (32,33). A motion recorder, a Timex watch (Timex, Waterbury, CT, U.S.A.) with the time mechanism removed so that each limb movement advanced the time hand of the watch, was worn to record activity during sleep. The watch's reading was recorded at bedtime and at rise time. A daily sleep log was also given to the participants. During the first and fifth weeks of the study, participants were asked to record the time they went to bed and woke up each day for 7 days. In addition, the patients recorded ratings on a 10-point Likert scale on their symptoms of pain, fatigue, and stiffness. The physician's assessment was made by a rheumatologist who was blinded to the participant's group assignment. This assessment included the participant's illness and medication use and tender points and pain as assessed by a dolorimeter (Wagner Force Dial FDK 20) with the American College of Rheumatology 1990 criteria for fibromyalgia (3). The point pressure threshold was mea-

sured by exerting increasing force for 1 kg/sec over the 18 tender point sites. The dolorimeter test was performed at the beginning and end of the study. Saliva samples collected before the first and last sessions were assayed for substance P. In most studies, substance P was more concentrated in saliva than in serum or plasma. Therefore, it appears that substance P does not merely "leak" from serum into saliva, but actively enters saliva by an unknown mechanism. Mean values for salivary substance P levels have been noted to range between 9.6 and 220 pg/mL in normal control participants (34). Saliva was obtained from a cotton dental swab coated with lemonade crystals by placing it in the participant's mouth until it was saturated with saliva. The saliva was then transferred into a microcentrifuge tube with a syringe and frozen for later analysis at Children's Hospital of Philadelphia.

#### RESULTS

Analyses of variance and posthoc Bonferroni  $t$  tests were conducted to compare the two groups on the self-report anxiety and depressed mood questionnaires, with the before and after treatment ses-

TABLE 1. Mean before and after massage therapy session measures (standard deviations in parentheses)

Measure (range of scores)	First day of massage		First day of relaxation		Last day of massage		Last day of relaxation	
	Before	After	Before	After	Before	After	Before	After
Anxiety (STAI) (0-80)	43.7 (9.5)	30.2 <sup>4</sup> (7.1)	41.9 (8.5)	33.4 <sup>3</sup> (7.5)	38.7 (12.8)	31.1 <sup>2</sup> (11.2)	40.0 (6.9)	29.2 <sup>4</sup> (6.7)
Depressed mood (POMS) (0-60)	10.0 (9.9)	3.3 <sup>2</sup> (4.1)	11.0 (9.2)	4.5 <sup>3</sup> (5.1)	5.9 (7.7)	2.8 <sup>2</sup> (4.5)	7.5 (6.7)	1.8 <sup>2</sup> (3.2)

STAI, State Trait Anxiety Index; POMS, Profile of Mood States.

\*Significant differences before versus after session on first day are indicated by superscripts in column 2 for the massage group and column 4 for the relaxation group. Significant differences before versus after session on the last day are indicated by superscripts in column 6 for the massage group and column 8 for the relaxation group (significance levels: <sup>1</sup> $p < .05$ , <sup>2</sup> $p < .01$ , <sup>3</sup> $p < .005$ , <sup>4</sup> $p < .001$  for one-tailed  $t$  tests).

**TABLE 2. Means for longer-term effects of massage therapy versus relaxation therapy (standard deviations in parentheses)**

Measure (range of scores)	First day of massage	Last day of massage	First day of relaxation	Last day of relaxation
Depression (CES-D) (0–60)	18.0 (9.2)	12.3 <sup>1</sup> (9.5)	17.7 (8.7)	17.1 (5.3)
Sleep hours (0–10)	5.8 (1.1)	6.4 <sup>1</sup> (1.1)	5.6 (1.3)	6.2 (.8)
Sleep movements (Motion recorder) (20–120)	101.3 (57.5)	83.3 <sup>1</sup> (52.8)	86.1 (45.5)	74.6 (24.8)
<b>Symptoms</b>				
Pain (0–10)	6.0 (3.2)	3.7 <sup>4</sup> (2.9)	7.7 (1.6)	6.3 (3.0)
Fatigue (0–10)	8.2 (1.7)	4.4 <sup>4</sup> (3.1)	8.5 (1.3)	7.4 (3.0)
Stiffness (0–10)	6.2 (3.3)	3.5 <sup>3</sup> (2.9)	7.6 (2.5)	7.2 (1.9)
Physician assessment of disease (0–3)	2.2 (.6)	1.7 <sup>1</sup> (.9)	2.5 (.8)	2.3 (.9)
Physician assessment of pain (Dolorimeter) (0–8)	4.5 (1.8)	3.3 <sup>1</sup> (2.6)	5.3 (2.0)	4.8 (1.7)
Number of tender points (0–18)	15.4 (1.7)	10.5 <sup>3</sup> (6.1)	16.1 (2.2)	14.6 (4.0)
Substance P (10–220)	84.1 (74.8)	69.2 <sup>1</sup> (66.4)	71.9 (55.4)	111.1 <sup>3</sup> (74.4)

CES-D, Center for Epidemiological Studies Depression Scale.

\*Superscripts reflect significance levels for significantly greater first day to last day changes for massage group (column 2) vs. relaxation group (column 4) (significance levels, <sup>1</sup> $p < .05$ , <sup>2</sup> $p < .01$ , <sup>3</sup> $p < .005$ , <sup>4</sup> $p < .001$  for one-tailed  $t$  tests).

sions being the repeated measures. As can be seen in Table 1, both groups showed decreased anxiety and depressed mood after the first and last sessions.

Repeated measures analyses of variance with first day and last day as the repeated measure were also conducted to compare the two groups with regard to: a) the depression questionnaire; b) the sleep measures (hours and movements); c) the physician's assessment of the disease, pain, and tender points; and 4) the substance P levels. As can be seen in Table 2, across the course of the study, the massage therapy group as compared with

the relaxation therapy group experienced decreased depression, improved sleep (a greater number of hours sleeping and fewer sleep movements), decreased symptoms (including pain, fatigue, and stiffness), improved assessments by the physician (on course of disease and pain), a decrease in the number of tender points, and a reduced substance P level.

## DISCUSSION

The decrease in anxiety and depressed mood after massage therapy and relaxation therapy was not surprising given that these changes were noted in our previ-

ous study on fibromyalgia (22) and in our other massage and relaxation therapy studies (35). The patients' reports of less depression, pain, stiffness, and fatigue were also consistent with our previous findings after massage therapy with fibromyalgia (22) and with other chronic pain conditions including migraine headaches, premenstrual syndrome, lower back pain, and chronic fatigue syndrome (35). Using a motion recorder, we were able to measure sleep activity more objectively in this study, and that measure confirmed the previous finding of less difficulty sleeping (22). Less diffi-



culty sleeping and less sleep activity may have contributed to the decrease in substance P (22). Finally,

*Using a motion recorder,  
we were able to measure  
sleep activity. . .*

the physicians' assessment of the improved clinical condition and their dolorimeter assessment of less pain replicated our previous findings and highlight the clinical significance of using massage therapy as a complementary treatment.

Future studies may use a sham massage therapy group (e.g., massage with no pressure) as an attention and touch control group. The relaxation therapy in the current study may have required more initiative and compliance, and therefore could be considered not equivalent to the massage therapy in its demands on participants. In addition, follow-up assessments may be conducted in future studies to determine any longer-term effects of the massage therapy. Further, it would be important to compare massage therapy with other therapies that have been effective with fibromyalgia, including cognitive behavior therapy (36) and other complementary therapies such as acupuncture (37) and electroencephalograph-driven stimulation (38).

### Acknowledgments

The authors thank the men and women who participated in this

study and the massage therapists who assisted with this study.

### REFERENCES

1. Bennett RM. Emerging concepts in the neurobiology of chronic pain: evidence of abnormal sensory processing in fibromyalgia. *Mayo Clin Proc* 1999;74:385-98.
2. Goldenberg DL. Fibromyalgia syndrome a decade later: what have we learned? *Arch Intern Med* 1999;159:777-85.
3. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990;33:160-72.
4. Henriksson C, Liedberg G. Factors of importance for work disability in women with fibromyalgia. *J Rheumatol* 2000;27:1271-6.
5. Bagge E, Bengtsson B, Carlsson L, et al. Low growth hormone secretions in patients with fibromyalgia. *J Rheumatol* 1998;25:145-8.
6. Turk DC, Okifuji A, Sinclair JD, et al. Pain, disability, and physical functioning in subgroups of patients with fibromyalgia. *J Rheum* 1996;23:1255-62.
7. Moldofsky H. A chronobiologic theory of fibromyalgia. *J Musc Pain* 1993;1:49-59.
8. Russell IJ, Orr MD, Littman B, et al. Elevated cerebrospinal fluid levels of substance P in patients with fibromyalgia syndrome. *Arthritis Rheum* 1994;37:1593-601.
9. Bennett RM. The origin of myofascial pain: an integrated hypothesis of focal muscle changes and sleep disturbance in patients with the fibromyalgia syndrome. *J Musc Pain* 1993;1:95-112.
10. Schroder HD, Drewes AM, Andreassen A. Muscle biopsy in fibromyalgia. *J Musc Pain* 1993;1:165-9.
11. Bennett RM, Clark SR, Campbell SM, et al. Low levels of somatomedin C in patients with the fibromyalgia syndrome. A possible link between muscle and pain. *Arthritis Rheum* 1992;35:1113-6.
12. Juhl JH. Fibromyalgia and the serotonin pathway. *Altern Med Rev* 1998;3:367-75.
13. Russell IJ, Michalek J, Vipraio J, et al. Platelet 3H-imipramine uptake receptor density and serum serotonin levels in patients with fibromyalgia/fibrositis symptoms. *J Rheumatol* 1992;19:104-19.
14. Gowans SE, deHueck A, Voss S, et al. A randomized, controlled trial of exercise and education for individuals with fibromyalgia. *Arthritis Care Res* 1999;12:120-8.
15. Beckelew SP, Conway R, Parker J, et al. Biofeedback/relaxation training and exercise interventions for fibromyalgia: a prospective trial. *Arthritis Care Res* 1998;11:196-209.
16. Wigers SH, Stiles TC, Vogel PA. Effects of aerobic exercise versus stress management treatment in fibromyalgia: a 4.5 year prospective study. *Scand J Rheumatol* 1996;25:77-86.
17. Blunz KL, Rajwani MR, Guerriero RC. The effectiveness of chiropractic management of fibromyalgia patients: a pilot study. *J Manip Phys Therapy* 1997;20:389-99.
18. Sim J, Adams N. Physical and other non-pharmacological interventions for fibromyalgia. *Baillieres Best Pract Res Clin Rheumatol* 1999;13:507-23.
19. Berman BM, Swyers JP, Ezzo J. The evidence for acupuncture as a treatment for rheumatological conditions. *Rheum Dis Clin North Am* 2000;26:103-15.
20. Finestone HM, Stenn P, Davies F, et al. Chronic pain and health care utilization in women with a history of childhood sexual abuse. *Rehabilitation* 2000;39:93-100.
21. Bellometti S, Galzigna L. Function of the hypothalamic-adrenal axis in patients with fibromyalgia syndrome undergoing mud-pack treatment. *Intl J Clin Pharmacol Res* 1999;19:27-33.
22. Sunshine W, Field TM, Quintino O, et al. Fibromyalgia benefits from massage therapy and transcutaneous electrical stimulation. *J Clin Rheumatol* 1996;2:18-22.
23. Ironson G, Field TM, Scafidi F, et al. Massage therapy is associated with the enhancement of the immune system's cytotoxic capacity. *Int J Neurosci* 1996;84:205-17.
24. Russell IJ. Neurohormonal aspects of fibromyalgia syndrome. *Rheum Dis Clin North Am* 1989;15:149-68.
25. Yunus MB, Masi AT. Juvenile primary fibromyalgia syndrome: a clinical study of thirty-three patients and matched normal controls. *Arthritis Rheum* 1985;28:138-45.
26. Spielberger CD, Gorsuch RC, Lushene RE. *The state trait anxiety inventory*. Palo Alto: Consulting Psychologists Press, 1970.
27. McNair DM, Lorr M, Droppelman LF. *POMS-profile of mood states*. San Diego: Educational and Industrial Testing Service, 1971.
28. Pucht D, Haskell D, McNair D. Predictors and patterns of change associated with the course of time-limited psychotherapy. *Archives of General Psychol* 1969;21:546-52.
29. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *J Appl Psychological Measurements* 1977;1:385-401.
30. Radloff L. The use of the center for epidemiological studies depression scale in adolescents and young adults. *J Youth Adol* 1991;20:149-65.
31. Radloff L, Locke BZ. The community mental health assessment survey and the CES-D scale. In: Weissman M, Myers J, Ross C, editors. *Community surveys of psychiatric disorders*. New Brunswick, NJ: Rutgers University Press, 1986:21-35.
32. Myers JK, Weissman MM. Use of self-report symptoms scale to detect depression in a community sample. *Am J Psychiatry* 1980;137:1081-3.
33. Weissman MM, Sholomskas D, Pottenger M, et al. Assessing depressive symptoms in five psychiatric populations: a validation study. *Am J Epidemiol* 1977;106:203-14.
34. Fischer HP, Eich W, Russell IJ. A possible role for saliva as a diagnostic fluid in patients with chronic pain. *Sem Arthritis and Rheum* 1998;27:348-59.
35. Field T. Massage therapy effects. *Am Psychologist* 1998;53:1270-81.
36. Friedburg F, Jason LA. Chronic fatigue syndrome and fibromyalgia: clinical assessment and treatment. *J Clin Psychol* 2001;57:433-55.
37. Ebell M. How effective are complementary/alternative medicine. *J Family Pract* 2001;50:400-1.
38. Mueller HH, Donaldson CCS, Nelson DV, et al. Treatment of fibromyalgia incorporating EEG-driven stimulation: a clinical outcomes study. *J Clin Psychol* 2001;57:933-52.