Original Research

Psychotherapy With Somatosensory Stimulation for Endometriosis-Associated Pain

A Randomized Controlled Trial

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OBJECTIVE: To evaluate whether psychotherapy with somatosensory stimulation is effective for the treatment of pain and quality of life in patients with endometriosis-related pain.

METHODS: Patients with a history of endometriosis and chronic pelvic pain were randomized to either psychotherapy with somatosensory stimulation (ie, different techniques of acupuncture point stimulation) or wait-list control for 3 months, after which all patients were treated. The primary outcome was brain connectivity assessed by functional magnetic resonance imaging. Prespecified secondary outcomes included pain on 11-point numeric rating scales (maximal and average global pain, pelvic pain, dyschezia, and dyspareunia) and physical and mental quality of life. A sample size of 30 per group was planned to compare outcomes in the treatment group and the wait-list control group.

RESULTS: From March 2010 through March 2012, 67 women (mean age 35.6 years) were randomly allocated to intervention (n=35) or wait-list control (n=32). In comparison with wait-list controls, treated patients showed improvements after 3 months in maximal global pain (mean group difference −2.1, 95% confidence interval [CI] −3.4 to −0.8; P=.002), average global pain (−2.5, 95% CI −3.5 to −1.4; P<.001), pelvic pain (−1.4, 95% CI −2.7 to −0.1; P=.036), dyschezia (−3.5, 95% CI −5.8 to −1.3; P=.003), physical quality of life (3.8, 95% CI 0.5–7.1, P=.026), and mental quality of life (5.9, 95% CI 0.6–11.3; P=.031); dyspareunia improved nonsignificantly (−1.8, 95% CI −4.4 to 0.7; P=.150). Improvements in the intervention group remained stable at 6 and 24 months, and control patients showed comparable symptom relief after delayed intervention.

CONCLUSION: Psychotherapy with somatosensory stimulation reduced global pain, pelvic pain, and dyschezia and improved quality of life in patients with endometriosis. After 6 and 24 months, when all patients were treated, both groups showed stable improvements.

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Endometriosis is a common gynecologic disorder that affects 6–10% of women of reproductive age and frequently leads to chronic pain and infertility.[1,2] Despite decades of research, the disease mechanisms are poorly understood. In particular, the weak correlation between the severity of organic pathology and reported pain intensity still puzzles clinicians and scientists alike.[3]

Systemic hormonal therapy improves pain symptoms, but recurrence rates are high after the medication

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is discontinued. There is also significant improvement in pain after surgical treatment. However, 30–60% of women show persistent or recurring pain after surgery.[1,2]

A recent consensus statement on endometriosis has concluded that endometriosis should best be examined in the context of chronic pain conditions.[4] With respect to therapeutic approaches, this implies that psychotherapeutic interventions could be effective in the treatment of endometriosis, preferably combined with other elements of multimodal pain therapy.

A retrospective case study provided first evidence that a combination of psychotherapy and somatosensory stimulation, that is, different techniques to stimulate acupuncture points, could be effective in improving pain and infertility associated with endometriosis.[5] The present study further investigated the effects of this integrative psychotherapeutic intervention for endometriosis-associated pain. We report the clinical study outcomes (secondary outcomes), which were collected in addition to changes in brain function (primary outcomes, reported in a separate manuscript).

MATERIALS AND METHODS

The experimental treatment was evaluated in an unblinded, randomized, wait-list controlled design for 3 months, after which patients in both comparison groups were treated. The study was approved by the institutional review board of the Technische Universität München (Munich, Germany; project number 2700/10). All patients provided written informed consent. The trial is registered at ClinicalTrials.gov (NCT01321840).

Eligible patients were adult females aged 18–40 years with a history of histologically verified endometriosis and chronic pelvic pain. Exclusion criteria were hormonal treatment during the month before enrollment, drug or alcohol addiction, pregnancy, insufficient knowledge of German language, and contraindications for magnetic resonance imaging (as a result of the primary outcome).

Allocation to treatment or control was implemented by using a telephone randomization procedure based on a computer-generated randomization list prepared by an investigator not involved in patient care (K.M.). Clinical examinations were performed at baseline and after 3 and 6 months at the Departments of Neuroradiology (C.P.) and Gynecology (R.M.P., B.d.O.) of the Technische Universität München and in a gynecologic practice (R.M.P., Munich). A long-term follow-up after 24 months was performed by sending out questionnaires. All study questionnaires were collected and analyzed at the Institute of Medical Psychology, Ludwig-Maximilians-Universität München (K.M., A.L., I.L.).

Patients in both groups were free to take acute pain medication, as required. Patients in the control group were cared for by the study gynecologists (R.M.P. and B.d.O.) by watchful waiting. The experimental treatment was performed in an outpatient setting by a medical specialist for psychosomatic medicine and traditional Chinese medicine (A.S.-A.). It combines elements of mindfulness-based psychotherapy,[6,7] hypnotherapy,[8] problem-solving therapy,[9] and cognitive–behavioral therapy.[10] It further uses techniques of somatosensory stimulation from traditional Chinese medicine such as acupuncture, moxibustion (heat), and cupping[11]. After completion of the randomized period, patients were encouraged to increase self-care at home, for example, by moxibustion of acupuncture points, herbal teas, or Qi Gong exercises.

A typical treatment session took 30–60 minutes. The topics of a single session arose from the current wishes and needs of a patient. The therapist started by asking the patient to report present worries and accompanying bodily sensations (eg, feelings of pressure, tension or pain in certain body areas). The therapist then used somatosensory stimulation in combination with psychotherapeutic techniques to resolve the current symptoms. For example, if a patient reported acute tension or pain in the lower abdomen while remembering a shameful situation in childhood, the therapist asked the patients for her inner needs while visualizing this situation and at the same time stimulated the acupuncture point CV3 (approximately 1.5 cm above the symphysis) by moxibustion. This typically induced immediate feelings of warmth in the lower abdomen and often led to spontaneous symptom relief. The strategy for somatosensory stimulation followed the principles of traditional Chinese medicine to balance for "yin" and "yang." The goal of each session was to render the patient into a stable and relaxed state free of pain and negative emotions by resolving intrusive memories of adverse life experiences (eg, death of a close relative or friend, sexual abuse, domestic violence). Psychotherapy was terminated when patients felt sufficient pain relief, had a baby, or when they wished to finish treatment as a result of nonresponse or long distance.

Predefined primary outcomes were changes in cortical thickness, functional connectivity, and perfusion of brain areas related to the processing of pain and emotions, as assessed by magnetic resonance imaging (results reported in an unpublished manuscript: Beissner F, Preibisch C, Schweizer-Arau A, Popovici RM, Meissner K. Psychotherapy with

somatosensory stimulation for endometriosis: the role of anxiety and the anterior hippocampus.). The predefined secondary outcomes comprised 1) maximal and average global pain, maximal pelvic pain, dyschezia, and dyspareunia as assessed by validated 11-point numerical rating scales ranging from "0" ("no pain") to "10" ("worst possible pain")[12,13]; 2) the proportion of patients with reduction of global pain by 50% or greater[13]; and 3) quality of life (physical and psychologic sum scores of the German version of the 12-Item Short-Form Health Survey[14]). In addition, validated questionnaires were used to assess functional well-being,[15] depression, and anxiety,[16,17] and patients were asked for acute pain medication.

Sample size calculations for both primary and secondary outcomes were based on unpaired two-tailed *t* tests assuming a power of 80% and a two-sided significance level of 5%. Regarding the most critical primary outcome, 24 participants per group would be required to detect a 5% difference between groups in gray matter as assessed by voxel-based morphometry.[18] To compensate for possible attrition, a sample size of 30 patients per group was planned to compare outcomes in the treatment group and the wait-list control group. Regarding the most important secondary outcome (pain scores), 16 patients per group would be necessary to detect a minimal clinically important difference for chronic pain of 2 points on an 11-point numeric rating scale[19] assuming a within-group standard deviation of 2 points.

Statistical analysis included one-way analysis of variance, paired *t* tests, Mann-Whitney *U* tests, and χ^2 tests, as appropriate. Cohen's *d* effect sizes of 0.8, 0.5, and 0.2 were considered as large, medium, and small,

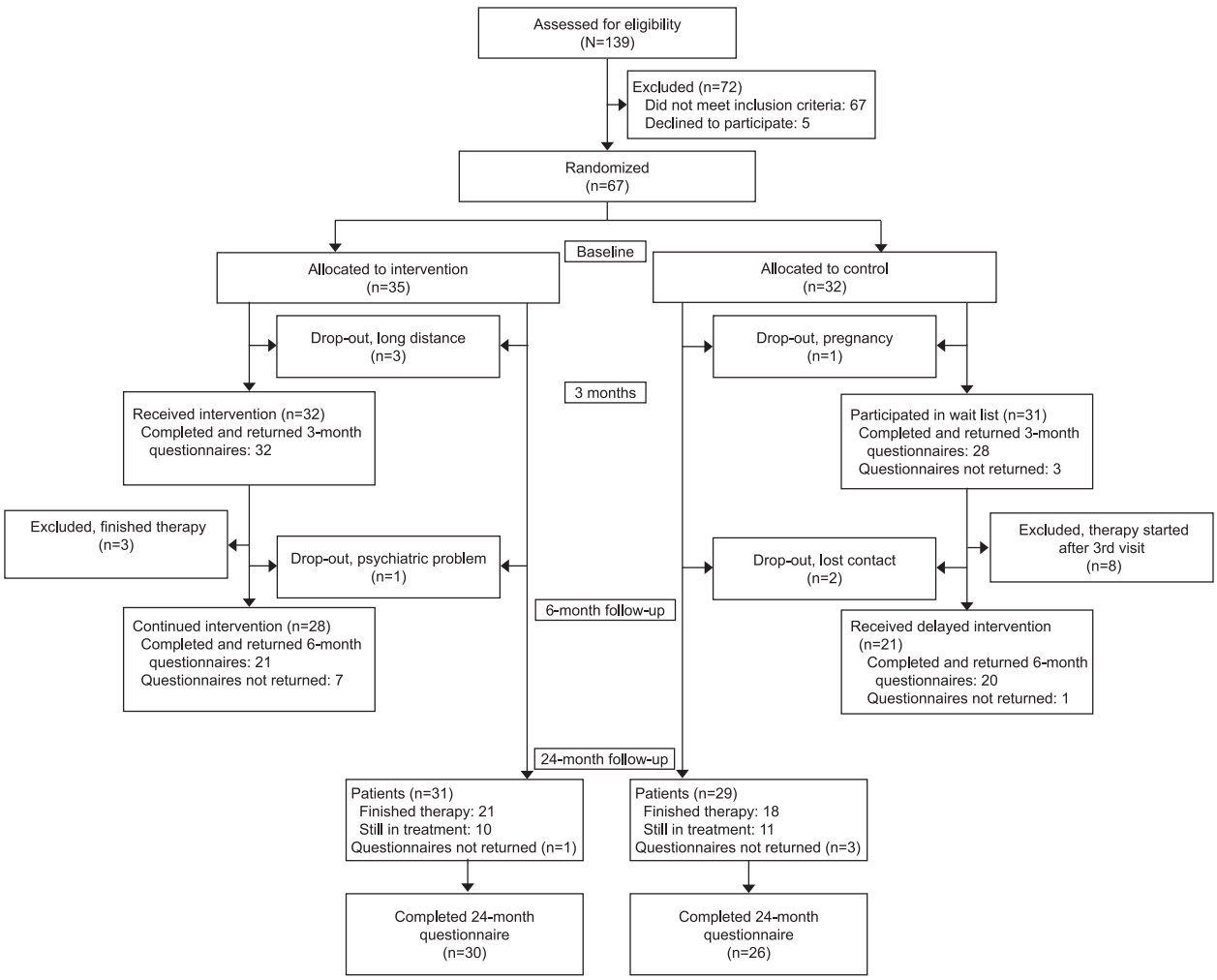

Fig. 1. Flowchart.

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respectively.[20] For all statistical tests, a *P* value of ≤.05 was considered significant. Analyses were performed by SPSS 23.

RESULTS

Between March 2010 and March 2012, 67 patients (mean age 35.6 years) with histologically verified endometriosis and moderate-to-severe pain were recruited and randomly allocated to intervention or wait-list control. At 3 months, data were available for 60 patients (90%). Follow-ups at 6 and 24 months included 41 patients (61%) and 56 patients (84%), respectively (Fig. 1).

Patients in the intervention and control groups were comparable with regard to all baseline characteristics, except for the physical score of quality of life, which was lower in control patients (Table 1). Sixty-one patients (91%) had undergone surgical treatment with complete or partial removal of endometriosis tissue, 29 patients (43%) at least twice.

The median number of interventions at 3 months for the patients in the intervention group was 8.5 (interquartile range 8–10). Improvements in maximal and average global pain ratings, pelvic pain, and dyschezia were larger in the intervention group than in the control group, whereas improvements in

Table 1. Demographic, Diagnostic, and Pain Characteristics of the Treatment and Control Group Participants

Variable	n	Treatment Group	n	Control Group	*P**
Age (y)	35	35.0 (33.3–36.6)	32	36.2 (34.5–37.9)	.285
BMI (kg/m^2)	33	21.7 (20.5–23.0)	32	23.1 (21.8–24.3)	.124
Endometriosis stage (ASRM score)	35		32		.252
I		4 (11)		3 (9)	
II		11 (31)		11 (34)	
III		8 (22)		13 (41)	
IV		12 (34)		5 (16)	
Pain duration greater than 5 y	35	27 (77)	32	27 (84)	.544
Last histologic confirmation of endometriosis (y)	35	2.1 (1.1–3.1)	32	3.3 (2.0–4.6)	.064
Surgical treatment during last laparoscopy	35		32		.627
Complete removal of endometriosis lesions		17 (49)		18 (56)	
Incomplete or no removal of endometriosis lesions		18 (51)		14 (44)	
Patients with infertility	35	27 (77)	32	24 (75)	1.000
Type of pelvic pain	35		32		.133
Cyclical pelvic pain		26 (74)		18 (56)	
Cyclical and noncyclical pelvic pain		9 (26)		14 (44)	
Pain outcomes (NRS, 0–10)					
Maximal global pain (past 4 wk)	35	7.3 (6.6–8.0)	32	7.7 (7.0–8.4)	.401
Average global pain (past 4 wk)	34	4.7 (4.0–5.4)	32	4.2 (3.5–4.9)	.288
Maximal pelvic pain (past 3 mo)	34	6.9 (6.2–7.6)	32	7.4 (6.7–8.3)	.328
Maximal dyschezia† (past 3 mo)	14	4.9 (3.3–6.5)	25	4.3 (3.0–5.4)	.487
Maximal dyspareunia‡ (past 3 mo)	12	4.9 (3.1–6.7)	19	5.2 (3.8–6.6)	.813
Use of analgesics	35		32		
NSAIDs		21 (60)		20 (63)	1.000
Opioids		3 (9)		2 (6)	1.000
Other		11 (31)		6 (19)	.272
Quality of life, well-being					
Physical health sum score (SF-12)	34	46.5 (43.9–49.0)	32	42.2 (39.6–44.8)	.020
Mental health sum score (SF-12)	35	40.6 (36.4–44.9)	32	40.9 (37.4–44.4)	.918
Functional well-being (FW-7)	35	18.5 (16.1–20.9)	31	19.0 (16.1–21.8)	.800
Depression, anxiety, stress					
Anxiety (HADS)	35	8.2 (6.9–9.7)	31	9.7 (8.4–11.0)	.121
Depression (HADS)	34	5.9 (4.9–7.0)	31	5.4 (4.3–6.4)	.466
Trait anxiety, stress (STAI)	32	43.7 (40.2–47.2)	29	48.1 (43.9–52.2)	.102

BMI, body mass index; ASRM, American Society for Reproductive Medicine; NRS, numeric rating scale; NSAIDs, nonsteroidal anti-inflammatory drugs; SF-12, 12-Item Short-Form Health Survey; FW-7, Functional Well-being; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.

Data are mean (95% confidence interval) or n (%) unless otherwise specified.

* Two-sided *t* test, Mann-Whitney *U* test, or χ^2 test.

† Based on patients who reported dyschezia greater than zero at one or more assessments.

‡ Based on patients who reported dyspareunia greater than zero at one or more assessments.

dyspareunia did not differ significantly from wait-list controls (Table 2; Appendix 1 [available online at http://links.lww.com/AOG/A875]). Fourteen patients in the intervention group (44%) but only one patient in the control group (4%) showed maximal global pain reduction by 50% or more ($P<.001$; Appendix 1 [http://links.lww.com/AOG/A875]). Days with nonsteroidal anti-inflammatory drugs per month decreased by 1.5 (median) in the intervention group (interquartile range −3.0 to 0.0), whereas a slight increase was observed in the control group (median 0.5, interquartile range 0.0–2.0; $P=.015$). The use of opioids and other pain medication remained stable in both groups ($P>.05$). Improvements of physical and mental quality of life, anxiety and depression scores, and functional well-being were significantly larger in the intervention group (Table 2; Appendix 1 [http://links.lww.com/AOG/A875]).

After 6 months, the median number of interventions from randomization to follow-up was 15 in the intervention group and 10 in the delayed intervention group (interquartile ranges 13.0–17.5 and 8.3–11.8, respectively). In the intervention group, improvements in maximal and average global pain, pelvic pain, dyschezia, and dyspareunia as well as quality of life, anxiety, depression, and well-being approximated those observed after 3 months (Table 3; Appendix 1 [http://links.lww.com/AOG/A875]). Eleven (57%) and 12 (53%) patients in the intervention and control groups, respectively, showed a reduction of maximal global pain by at least 50% (Appendix 1 [http://links.lww.com/AOG/A875]). After delayed intervention, improvements seen at 6 months were similar to those observed in the intervention group (Table 3; Appendix 1 [http://links.lww.com/AOG/A875]).

At 24 months, 35 of 56 patients (63%) with completed questionnaires had meanwhile finished treatment (20 intervention, 15 delayed intervention). The median number of interventions was 16.5 in the intervention group and 18.5 in the delayed intervention

Table 2. Changes From Baseline and Group Differences for Clinical Outcomes at 3 Months (At the End of the Randomized Period)

	Intervention		Wait-List Control				
Parameter	n	Mean Change (95% CI)	n	Mean Change (95% CI)	Mean Difference (95% CI)	*P**	Effect Size (Cohen's *d*)
Pain outcomes (NRS, 0–10)							
Maximal global pain (past 4 wk)	32	−3.0 (−3.8 to −2.1)	28	−0.9 (−1.8 to 0.1)	−2.1 (−3.4 to −0.8)	.002	0.87
Average global pain (past 4 wk)	31	−2.5 (−3.2 to −1.7)	28	−0.0 (−0.8 to 0.7)	−2.5 (−3.5 to −1.4)	<.001	1.18
Maximal pelvic pain (past 3 mo)	27	−2.4 (−3.3 to −1.5)	26	−1.0 (−1.9 to −0.1)	−1.4 (−2.7 to −0.1)	.036	0.55
Maximal dyschezia† (past 3 mo)	13	−3.1 (−4.9 to −1.3)	21	0.4 (−0.9 to 1.8)	−3.5 (−5.8 to −1.3)	.003	1.10
Maximal dyspareunia‡ (past 3 mo)	9	−2.9 (−5.0 to −0.9)	17	−1.1 (−2.6 to 0.4)	−1.8 (−4.4 to 0.7)	.150	0.61
Quality of life, well-being							
Physical health sum score (SF-12)	32	5.5 (3.2–7.8)	28	1.7 (−0.7 to 4.1)	3.8 (0.5–7.1)	.026	1.11
Mental health sum score (SF-12)	32	5.1 (1.4–8.8)	28	−0.8 (−4.8 to 3.1)	5.9 (0.6–11.3)	.031	0.57
Functional well-being (FW-7)	31	6.5 (3.0–9.9)	27	−1.7 (−5.5 to 2.0)	8.2 (3.1–13.3)	.002	0.85
Depression, anxiety, stress							
Anxiety (HADS)	31	−2.6 (−4.1 to −1.2)	28	0.0 (−1.5 to 1,5)	−2.6 (−4.7 to −0.6)	.012	0.68
Depression (HADS)	29	−2.5 (−3.3 to −1.7)	28	0.2 (−0.7 to 1.0)	−2.7 (−3.8 to −1.5)	<.001	1.19
Trait anxiety, stress (STAI)	29	−5.4 (−7.6 to −3.1)	24	−1.3 (−3.8 to 1.2)	−4.1 (−7.5 to −0.7)	.018	0.68

CI, confidence interval; NRS, numeric rating scale; SF-12, 12-Item Short-Form Health Survey; FW-7, Functional Well-being; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.

* Based on analysis of variance if not otherwise indicated.

† Based on patients who reported dyschezia greater than zero at one or more assessments.

‡ Based on patients who reported dyspareunia greater than zero at one or more assessments.

Table 3. Changes From Baseline at 6 Months (Both Comparison Groups Were Treated)

Parameter	Intervention n	Intervention Mean Change (95% CI)	Delayed Intervention n	Delayed Intervention Mean Change (95% CI)	Mean Difference (95% CI)	P*	Effect Size (Cohen's d)
Pain outcomes (NRS, 0–10)							
Maximal global pain (past 4 wk)	20	−2.9 (−3.9 to −1.9)	20	−3.7 (−4.7 to −2.7)	0.8 (−0.6 to 2.2)	.261	0.36
Average global pain (past 4 wk)	19	−2.6 (−3.6 to −1.5)	18	−2.3 (−3.3 to −1.2)	−0.3 (−1.8 to 1.2)	.683	0.13
Maximal pelvic pain (past 3 mo)	20	−3.4 (−4.7 to −2.2)	18	−3.3 (−4.6 to −1.9)	−0.2 (−2.0 to 1.6)	.823	0.07
Maximal dyschezia† (past 3 mo)	8	−4.8 (−7.0 to −2.8)	12	−2.0 (−3.7 to −0.3)	−2.9 (−5.6 to −0.1)	.040	1.10
Maximal dyspareunia‡ (past 3 mo)	4	−1.9 (−4.3 to 0.5)	11	−2.7 (−4.1 to −1.2)	−0.8 (−3.6 to 2.0)	.548	0.36
Quality of life, well-being							
Physical health sum score (SF-12)	21	5.9 (3.0–8.7)	20	7.4 (4.5–10.3)	−1.5 (−5.6 to 2.5)	.446	0.24
Mental health sum score (SF-12)	21	6.4 (1.5–11.4)	20	2.9 (−2.2 to 8.0)	3.5 (−3.6 to 10.6)	.329	0.31
Functional well-being (FW-7)	20	5.9 (2.9–8.9)	20	5.0 (2.0–8.0)	0.9 (−3.3 to 5.2)	.663	0.14
Depression, anxiety, stress							
Anxiety (HADS)	20	−3.2 (−4.8 to −1.6)	19	−2.3 (−4.0 to −0.7)	−0.9 (−3.2 to 1.4)	.438	0.25
Depression (HADS)	19	−2.9 (−4.3 to −1.6)	18	−1.9 (−3.3 to −0.6)	−1.0 (−2.9 to 0.9)	.288	0.35
Trait anxiety, stress (STAI)	19	−4.9 (−9.1 to −0.8)	17	−5.2 (−9.6 to −0.8)	0.3 (−5.7 to 6.4)	.914	0.04

CI, confidence interval; NRS, numeric Rating Scale; SF-12, 12-Item Short-Form Health Survey; FW-7, Functional Well-being; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.
* Based on analysis of variance.
† Based on patients reporting dyschezia greater than zero at one or more assessments.
‡ Based on patients reporting dyspareunia greater than zero at one or more assessments.

group (interquartile ranges 13–30.5 and 8–26, respectively). Results indicated sustained improvements of pain scores, responder rates, well-being, depression, and anxiety in both treatment groups (Tables 4 and 5; Appendix 2 [available online at http://links.lww.com/AOG/A875]). Seven patients had meanwhile undergone further surgery and one patient was taking hormonal drugs. Mean improvement in maximal global pain among these eight patients was slightly smaller at follow-up than in the remaining patients (mean difference −1.4, 95% confidence interval [CI] −3.9 to 1.1, P=.267). Eleven patients with pregnancy onsets during follow-up had meanwhile given birth to a neonate (eight intervention, three delayed intervention), and one patient (intervention) was pregnant. Improvement in maximal global pain among these 12 patients tended to be larger than in the remaining patients (−1.9, −4.0 to 0.2, P=.069).

DISCUSSION

We investigated the effects of psychotherapy with somatosensory stimulation on brain function (primary outcome) and clinical (secondary) outcomes in patients with a history of endometriosis and ongoing chronic pelvic pain. We focus on the secondary outcomes to evaluate the clinical effectiveness of this treatment in detail. Results at 3 months indicate that the treatment reduced pain to a clinically significant amount, going along with improvements in physical and mental quality of life, anxiety, depression, and functional well-being of moderate-to-large effect sizes. The improvements in the treatment group remained stable at 6 months, whereas patients in the former control group showed comparable symptom relief after delayed intervention. Follow-up data at 24 months, when more than two thirds of patients had finished the therapy, point to the long-term stability of the treatment effects. Furthermore, although not a predefined outcome measure, 60% of patients with a previous unfulfilled wish for a child at baseline had given birth to a healthy neonate at the time of follow-up.

Some limitations need to be addressed. We used retrospective pain ratings, which may have introduced recall bias. The results from the pain ratings, however,

Table 4. Changes From Baseline at 24 Months (Both Comparison Groups Were Treated)

Parameter	Intervention n	Intervention Mean Change (95% CI)	Delayed Intervention n	Delayed Intervention Mean Change (95% CI)	Mean Difference (95% CI)	*P**	Effect Size (Cohen's *d*)
Pain outcomes (NRS, 0–10)							
Maximal global pain (past 4 wk)	30	−4.1 (−5.3 to −2.9)	26	−3.0 (−4.3 to −1.7)	−1.1 (−2.8 to 0.7)	.227	0.33
Average global pain (past 4 wk)	28	−3.3 (−4.4 to −2.1)	26	−1.3 (−2.5 to −0.1)	−1.9 (−3.6 to −0.3)	.019	0.66
Maximal pelvic pain (past 3 mo)	29	−3.8 (−5.0 to −2.6)	26	−2.7 (−4.0 to −1.4)	−1.1 (−2.9 to 0.7)	.229	0.33
Maximal dyschezia† (past 3 mo)	12	−4.0 (−5.7 to −2.2)	20	−1.3 (−2.7 to 0.0)	−2.6 (−4.8 to −0.4)	.020	0.87
Maximal dyspareunia‡ (past 3 mo)	10	−4.8 (−7.4 to −2.2)	15	−2.6 (−4.7 to −0.5)	−2.2 (−5.5 to 1.1)	.175	0.60
Well-being							
Functional well-being (FW-7)	30	8.8 (6.1–11.5)	24	5.2 (2.2–8.3)	3.6 (−0.5 to 7.6)	.086	0.48
Depression, anxiety, stress							
Anxiety (HADS)	30	−3.0 (−4.4 to −1.5)	24	−2.5 (−4.1 to −0.9)	−0.5 (−2.7 to 1.7)	.673	0.12
Depression (HADS)	29	−2.9 (−4.1 to −1.7)	24	−1.3 (−2.7 to −0.0)	−1.6 (−3.3 to 0.2)	.085	0.49
Trait anxiety, stress (STAI)	27	−6.4 (−9.7 to −3.2)	23	−5.0 to (−8.5 to −1.5)	−1.4 (−6.2 to 3.4)	.557	0.17

CI, confidence interval; NRS, numeric rating scale; SF-12, 12-Item Short-Form Health Survey; FW-7, Functional Well-being; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.
* Based on analysis of variance.
† Based on patients reporting dyschezia greater than zero at one or more assessments.
‡ Based on patients reporting dyspareunia greater than zero at one or more assessments.

corresponded well with the results from validated questionnaires for the assessment of quality of life, well-being, depression, and anxiety, indicating that the patients experienced reliable improvements. Furthermore, to minimize social acceptability bias, all questionnaires were handed out and recollected by investigators, who were not involved in the treatment of study patients. As a result of difficulties in creating an equally credible placebo intervention for the complex and individualized treatment approach, we

Table 5. Changes From Baseline for Clinical Outcomes at 24 Months (All Patients Combined)

Parameter	n	Mean Change (95% CI)	*P**	Effect Size (Cohen's *d*)
Pain outcomes (NRS, 0–10)				
Maximal global pain (past 4 wk)	56	−3.6 (−4.4 to −2.7)	<.001	1.09
Average global pain (past 4 wk)	55	−2.3 (−3.0 to −1.3)	<.001	1.14
Maximal pelvic pain (past 3 mo)	55	−3.3 (−4.2 to −2.4)	<.001	1.02
Maximal dyschezia† (past 3 mo)	32	−2.3 (−3.5 to 1.2)	.005	0.73
Maximal dyspareunia‡ (past 3 mo)	25	−3.5 (−5.1 to 1.8)	<.001	0.87
Well-being (FW-7)				
Functional well-being (FW-7)	54	7.2 (5.1–9.3)	<.001	0.96
Depression, anxiety, stress				
Anxiety (HADS)	54	−2.8 (−3.8 to −1.7)	<.001	0.69
Depression (HADS)	53	−2.2 (−3.1 to −1.3)	<.001	0.66
Trait anxiety, stress (STAI)	50	−5.8 (−8.1 to −3.4)	<.001	0.70

CI, confidence interval; NRS, numeric rating scale; FW-7, Functional Well-being; HADS, Hospital Anxiety and Depression Scale; STAI, State-Trait Anxiety Inventory.
* Based on paired *t* test.
† Based on patients reporting dyschezia greater than zero at one or more assessments.
‡ Based on patients reporting dyspareunia greater than zero at one or more assessments.

compared active intervention with wait-list controls in a randomized design for 3 months. The major limitation of such a design is the lack of a placebo control group, and some of the improvement at the end of the randomized period may therefore be the result of positive expectation. Wait-list control groups, however, control for other important confounders such as regression to the mean, spontaneous improvement, and the effects of unidentified cointerventions.[21] It should be noted that a wait-list control group was only included for 3 months, after which patients in both comparison groups could be treated, and some of the improvement at 6 and 24 months could have happened without treatment.

Our trial does not allow to draw firm conclusions on the mechanisms underlying the observed improvements at 3 months. However, it may be assumed that, like in other pain conditions, both specific and nonspecific treatment components played a role.[22] Putative specific factors include the problem-solving approach, which helps to reduce the emotional burden of serious life events such as sudden death of a close relative, abuse, or parents as alcoholics. Such potentially traumatizing events are more frequently encountered in patients with endometriosis and pelvic pain than in the reference population.[23–26] A unique feature of the therapeutic approach studied here is the combination of psychotherapeutic techniques and somatosensory stimulation by means of acupuncture point stimulation. This could yield synergistic effects when compared with the separate application of each modality.[27] The importance of somatic stimulation during psychotherapy is also emphasized by a number of approaches using acupuncture point tapping, eye movements, and other somatic elements in combination with psychotherapy. Some of these therapies have recently demonstrated good results in trauma patients[28] and other psychologic disorders,[29] but also in chronic pain conditions, like fibromyalgia[30] and tension-type headache.[31] Nonspecific (placebo) effects may have further contributed to the total improvement of symptoms. Such effects are supposed to be large in individualized treatment approaches, like ours, in which the health care provider delivers a high amount of confidence, trust, and empathy.[32,33]

The therapeutic success of the intervention studied here underlines the importance of psychologic factors in the etiology of chronic endometriosis-associated pain as has been suggested previously.[23,24,34,35] Psychotherapeutic treatment approaches should be considered for endometriosis whenever a patient experiences chronic pelvic pain despite previous pharmacologic or surgical treatments or when a patient wishes to discontinue hormonal suppressive drugs as a result of side effects or the desire to have a child. A combination of psychotherapy and somatosensory stimulation appears to be particularly useful in this regard. Gynecologists should also consider asking patients for critical life events as part of routine history-taking.

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