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Craniosacral Therapy for the treatment of chronic neck pain: a randomized sham-controlled trial

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ABSTRACT

Objectives: With growing evidence for Craniosacral Therapy (CST) effectiveness for pain management, the question about CST efficacy remained unclear. This study therefore aimed at investigating CST in comparison to sham treatment in chronic non-specific neck pain patients.

Methods: 54 blinded patients were randomized to either 8 weekly units of CST or light touch sham treatment. Outcomes were assessed before and after treatment (week 8) and a further 3 months later (week 20). The primary outcome was pain intensity on a visual analogue scale; secondary outcomes included pain on movement, pressure pain sensitivity, functional disability, health-related quality of life, well-being, anxiety, depression, stress perception, pain acceptance, body awareness, patients' global impression of improvement and safety.

Results: In comparison to sham, CST patients reported significant and clinically relevant effects on pain intensity at week 8 (-21mm; 95%-CI: [-32.6|-9.4]; p=.001; d=1.02) as well as at week 20 (-16.8mm; 95%-CI: [-27.5|-6.1]; p=.003; d=0.88). Minimal clinically important differences in pain intensity at week 20 were reported by 78% of the CST patients, while 48% even had substantial clinical benefit. Significant differences at week 8 and 20 were also found for pain on movement, functional disability, physical quality of life and patients' global improvement. Pressure pain sensitivity and body awareness were significantly improved only at week 8; anxiety only at week 20. No serious adverse events were reported.

Discussion: CST was both specifically effective and safe in reducing neck pain intensity and may improve functional disability and quality of life up to 3 months post intervention.

Key words: Craniosacral Therapy, Manual Therapies, Neck Pain, Sham Treatment, Randomized Controlled Trial

INTRODUCTION

Neck pain is a significant public health problem with one in two people experiencing neck pain at least once in their lifetime.[1] Neck pain is often recurrent, of non-specific nature and associated with disability in both social and occupational life.[2-4] For the treatment of chronic courses evidence is still limited, as only therapeutic exercises, acupuncture and manual therapies were recommended in recent clinical practice guidelines.[5-7] When asking manual therapists about their perception and use of complementary and alternative medicine for the treatment of chronic pain conditions, one repeatedly mentioned treatment was Craniosacral Therapy (CST).[8]

CST is thought as a non-invasive, mindfulness-based treatment approach using gentle manual palpation techniques to release fascial restrictions between cranium and sacrum.[9] The craniosacral system anatomically encompasses the structures of the central nervous system including the skull, the cranial sutures, the cerebrospinal fluid and the membranes of the brain and spinal cord. It is influenced by and linked to the musculoskeletal system,[10] and presumably to the vascular and endocrine system as well as to the sympathetic and parasympathetic nervous system.[11] In craniosacral theory, fascial restrictions within the craniosacral system lead to abnormal, arrhythmic motion of the cerebrospinal fluid. This craniosacral rhythm is assessable by palpation and quantifiable by encephalogram, myelogram and magnetic resonance imaging.[12] There is also growing evidence for fascial involvement in pain chronification. Studies have shown increased activity of fascial nociceptors within restricted connective tissue, which can contribute to remodeling processes of inflammation and fibrosis, increased tissue stiffness, muscle tension and chronic pain.[13,14] However, research on craniosacral diagnostic and treatment mechanisms revealed very heterogeneous results,[11,12] with only preliminary evidence supporting inherent processes of peripheral and descending pain inhibition due to gentle fascial palpation techniques.[11,15,16]

Effectiveness of craniosacral treatment techniques on health outcomes has been shown for a number of chronic pain syndromes, but is limited to observational designs and randomized controlled trials with low to moderate methodological quality.[17-19] Efficacy studies have not been realized to date as well as studies on musculoskeletal pain,[20] although neck and back pain were the most frequent complaints CST was requested for.[21] Therefore, this study aimed at investigating the efficacy of CST on chronic non-specific neck pain in comparison to a manual sham control intervention.

MATERIALS AND METHODS

Trial Design and Registration

The study was designed as a randomized controlled clinical trial with parallel group design and 3 months of follow-up observation. After baseline assessment patients were randomized to either a CST group or an active attention-control group receiving light touch sham treatment. Outcome measures were collected at week 8 after randomization (post intervention) and week 20 after randomization (3-month follow-up). The trial was conducted between February 2012 and May 2013 at the Department of Internal and Integrative Medicine, Kliniken Essen-Mitte, University of Duisburg-Essen, Essen, Germany. Prior to patient recruitment, the trial protocol was approved by the ethics committee of the University of Duisburg-Essen, Germany (11-4850-BO) and registered at ClinicalTrials.gov (NCT01526447).

Randomization

A statistician, who was not involved in conducting the study, generated a non-stratified random allocation sequence with randomly varying block lengths using the random number generator RANUNI from SAS/STAT software (release 9.2, SAS Inc., USA). Based on these random number tables he prepared sealed and opaque envelopes sorted in ascending order of randomization. To reveal patient's group assignment, the envelope with the lowest number was opened directly after each baseline assessment by the trial coordinator who neither was involved in the random sequence generation nor in the assessment of study outcomes.

Sample Criteria

Patients were recruited from specialist care, primary care and non-care populations via advertisements. To assess eligibility, those who called in were screened by a research assistant, whereupon eligible patients obtained written study information and a physical and neurological examination by a study physician. If all eligibility criteria were met, patients had to give written inform consent and were included in the study.

Inclusion criteria were an age of 18 to 65, chronic non-specific neck pain for 3 months or more with at least moderate pain intensity of ≥45 mm on a 100 mm visual analogue scale (VAS)[22], and treatment naïvety with respect to CST. Participation was not possible in cases of specific neck pain due to degenerative diseases (disc prolapse, scoliosis), inflammatory diseases (spondylitis, arthritis), neurological diseases (neuropathy, multiple sclerosis), physical traumata (whiplash, operation at the cervical spine), or neoplasms of the spine. Severe comorbid somatic and psychiatric disorders such as oncological diseases or major depression as well as current

pregnancy also were exclusion criteria. Patients taking corticosteroids, opiates, muscle relaxants, antidepressants or with recently initiated or modified drug therapy or invasive/manipulative treatment were also excluded.

Sample size was calculated on the basis of pain intensity ratings of chronic non-specific neck-pain patients who received osteopathic manipulative treatment[23] using G*Power software (release 3.1.3, Kiel University, Germany).[24] To detect an expected group difference of 1.73 ± standard deviation (SD) of 2.16 on a 10-point numeric rating scale (effect size of 0.84) with a power of 80%, a two-sided t-test with α=5% significance level required 24 patients per group. Accounting a possible loss of statistical power due to patient withdrawal of 10%, a total sample size of 54 patients was calculated.

Blinding

First, patients were blinded to group allocation and to the fact that one group would receive sham treatment as it was recommended for manual therapy trials;[25] instead they were told that two different CST techniques would be tested. Second, investigators assessing outcomes remained blind to patients' group allocation during the whole study period. Third, the statistician who conducted outcome analyses was blinded to group allocation by renaming groups with numbers.

Interventions

Standardized treatment protocols comprised 8 units of CST or sham treatment once a week lasting 45 minutes each. Patients of both groups received initial structural CST examination, which was repeated at the end of each unit, and were treated by one of four licensed physiotherapists with advanced CST qualification and on average 6 years of clinical practice. Treatment steps were recorded by therapists using a structured log.

Treatment group: The CST protocol was designed to release restrictions of the cranium and spine up to the pelvis and sacrum using standardized application of gentle fascial traction, release and unwinding techniques in accordance with the respective palpated restrictions.[26,27] Applied techniques included: Frontal and parietal lift, medial compression of the parietal bones, release of the sagittal suture and atlanto-occipital joint, compression-decompression of the sphenobasilar and temporomandibular joints, cranial base release, release of the hyoid diaphragm and thoracic inlet, dural tube traction, respiratory and pelvic diaphragm release, lumbosacral and sacroiliac decompression, fascial unwinding of the neck/shoulders and lower limbs, and still point induction.[9,15] If indicated, dialogue techniques for increasing body awareness and assisting the process of somato-emotional release were used.[28]

Sham control group: The sham protocol was designed to be credible but not specifically effective. Therefore, light touch was applied on standardized anatomic areas, equal to those treated with CST, for two minutes each time.[29,30] In addition, body awareness instructions were given to simulate CST dialogue techniques.

Outcome Measures

The primary outcome was average pain intensity during the last 7 days recorded on a 100 mm VAS.[31] Secondary outcomes were pain on movement, pressure pain sensitivity, neck pain-related disability, health-related quality of life, well-being, anxiety and depression, stress perception, pain acceptance, body connection, patients' global impression of improvement, and safety.

To assess pain on movement, patients obtained the Pain on Movement Questionnaire (POM) and were asked to rate pain intensity on a 100 mm VAS while flexing, extending, laterally flexing and laterally rotating their head. An average pain on movement score was then calculated from all movement directions.[32] Pressure pain sensitivity was measured at the individual point of maximum pain and bilaterally at anatomically predefined sites (levator scapulae, trapezius and semispinalis capitis muscle). For these points, pressure pain thresholds (PPT) were determined 3 times each using a digital algometer (Somedic AB, Hörby, Sweden) with a 1 cm^2 cylinder. Pressure was applied in steps of 40 kPa/s until patients stated pain in addition to pressure.[33,34] Functional disability was assessed using the Neck Disability Index (NDI), a 10-item questionnaire that enquired the disability in daily activities induced by neck pain. Scores of less than 9 indicate no perceived disability, 10 – 29 mild disability, 30 – 49 moderate disability, 50 – 69 severe disability, and 70 – 100 complete disability.[35] Health-related quality of life was assessed on two subscales, physical and mental quality of life, using the 12-item Short Form Health Survey (SF-12). Subscales were standardized to a mean of 50 ± SD of 10 and a range of 0 to 100 with 0 indicating the lowest level and 100 the highest level of health.[36] Well-being was measured by the sum score of the 16-item Questionnaire for Assessing Subjective Physical Well-being (FEW-16).[37] Anxiety and depression were measured using the Hospital Anxiety and Depression Scale (HADS). Each subscale is composed of 7 items with a maximum of 21 points. Scores below 8 indicating anxiety and depression levels within the normal limits, 8 – 10 points subclinical levels, and over 10 points a possible clinical disorder.[38] To assess stress perception, patients obtained the Perceived Stress Questionnaire (PSQ) in the 20-item version.[39] Pain acceptance was measured by the 8-item Positive Life Construction Scale of the Emotional/Rational Disease Acceptance Questionnaire (ERDA).[40] Body connection was measured by the Scale of Body Connection (SBC), which is composed of two subscales, body awareness and body dissociation.[41] Patients' ratings of their Global Impression of Improvement (PGI-I) were assessed on a 7-point scale from 1 (very much improved) to 7 (very

much worse).[42,43] Safety assessment was realized by asking patients at the beginning of each treatment unit about the frequency and severity of side effects. In addition, patients were requested to document side effects as well as concurrent treatment and medication use in a daily log.

Furthermore, treatment expectancy was assessed as part of the Credibility/Expectancy Questionnaire (CEQ) on a 9-point rating scale from 1 (not at all) to 9 (very much).[44,45] Treatment credibility and quality of the therapeutic alliance, measured by the Helping Alliance Questionnaire (HAQ),[46] were analyzed and reported separately.[47]

Statistical Analysis

All analyses were based on the intention-to-treat population including all patients who were initially randomized, regardless of whether they had missing data or were not fully adhering to the treatment protocol. Missing at random values were imputed 20 times using fully conditional specification iterations, a multiple imputation technique based on multivariate regression models of baseline values and socio-demographic parameters.

Drop-out analyses and baseline comparability were analyzed using independent samples t-tests for continuous data and chi-square tests for categorical data. Concurrent medication use was converted into defined daily doses (DDD)[48] and analyzed using repeated measures analysis of covariance (ANCOVA) with treatment group as classified factor and patients' expectations as linear covariate. Primary outcome was analyzed as a function of treatment group (classified factor), patients' expectations and respective baseline values (linear covariates) using univariate ANCOVA. Between-group differences (Δ) and 95% confidence intervals (CI) were estimated using two-sided t-tests and an alpha level of 5%. Equal models were applied for secondary outcomes, which were analyzed exploratory. This way, no alpha level adjustment for multiple testing was necessary.[49] For each outcome, standardized effect sizes (Cohen's d) were calculated by dividing estimated group differences by the pooled SD at baseline. In addition, responder analyses were calculated for patients who improved at least 20% of their respective baseline values (minimal clinically important difference) and for ones with at least 50% improvement (substantial clinical benefit).[50,51] Between-group differences for treatment response analyses were tested with chi-square tests. All analyses were performed using SPSS software (release 22.0, IBM, USA).

RESULTS

Patient Recruitment and Flow

Figure 1 displays the Consort flow chart of patient recruitment and loss during the study period. Out of 150 initially interested patients, 96 had to be excluded because of not fulfilling eligibility criteria or reporting scheduling problems. In total, 54 patients were randomized and allocated to one of the two treatment groups.

While 4 patients from the CST group and 8 patients from the sham group did not attend all treatment units provided, only 3 patients were lost to assessment at week 8. Reasons for drop-out were scheduling problems and loss of interest. At week 20, drop-out of 7 patients had to be recorded due to scheduling problems, while 2 others made no further reply. Comparisons of patients who completed the study with those who were lost to week 8 and week 20 revealed no significant differences concerning their social-demographics, neck pain characteristics and treatment expectancy ($p \geq .05$) (table 1).

Sample characteristics at baseline

Patients' baseline characteristics are shown in table 2. Their age ranged from 19 to 65 with a mean of 44.6 ± 10.0 years. All were Caucasians. Most were female (81.5%), employed and of normal body mass index. The sample included patients from all educational levels, which were equally distributed. Patients reported 9.6 ± 8.9 years of neck pain duration, with most of them had received several pharmacological and non-pharmacological treatments during that time. No significant differences on patients' social demographics and neck pain characteristics were found between study groups ($p \geq .05$). Patient's expectations that CST would be successful in reducing their neck pain symptoms were also comparable between groups ($p \geq .05$).

Concurrent Treatments

Patients' use of concurrent pain medication is illustrated in figure 2. During the 8 weeks of treatment, the average intake of analgesics was 0.1 ± 0.1 DDD in the CST group and 0.5 ± 0.3 DDD in the sham group. Analysis revealed no significant main effect of time ($p = .716$) and group ($p = .099$), and no significant time-group interaction ($p = .069$). Other concurrent treatments were reported by 5 patients of the sham group who used massage 4 times and acupuncture 2 times.

Primary Outcome

Effects on the primary outcome are shown in table 3. In comparison to sham, patients of the CST group reported significant less pain intensity of $\Delta = -21.0$ mm at week 8 (95% CI: [-32.6|-9.4]; $p = .001$; $d = 1.02$) as well as $\Delta = -16.8$ mm at week 20 (95% CI: [-27.5|-6.1]; $p = .003$; $d = 0.88$).

A minimal clinically important pain reduction of at least 20% was reported by 74.1% of the CST patients versus 40.7% of the sham patients at week 8 ($p = .013$); and 77.8% of the CST patients versus 51.9% of the sham patients at week 20 ($p = .046$). Substantial clinical benefit of at least 50% pain relief at week 8 was reported by 44.4% of the CST patients versus 14.8% of the sham patients ($p = .017$). At week 20, the comparison of 50%-response rates did not reach the level of significance ($p = .091$) (table 4).

Secondary Outcomes

Analyses of secondary outcomes are also shown in table 3. At week 8, significant between-group differences were detected for pain on movement (p=.001; d=0.92), pressure pain thresholds at the point of maximum pain (p=.038; d=0.52) and bilaterally at the trapezius muscle (p=.042; d=0.43), functional disability (p=.010; d=0.73), physical quality of life (p=.013; d=0.64), body awareness (p=.001; d=0.59), and global improvement (p=.000; d=1.01). At week 20, significant effects could be detected for pain on movement (p=.020; d=0.66), functional disability (p=.006; d=0.80), physical quality of life (p=.000; d=1.07), and global improvement (p=.029; d=0.62). Although anxiety and depression levels were reduced in the CST group and increased in the sham group, between-group comparisons were only significant for anxiety and only at week 20 (p=.020; d=0.58). No significant group differences were found for stress perception, well-being, mental quality of live, pain acceptance and body dissociation ($p \geq .05$).

Safety

No serious adverse events were reported. Minor side effects during or subsequent to the treatment were reported by 6 patients of the CST group and included increased neck pain in 2 patients and complaints in the jaw area, shivering, tiredness, strong emotional reactions and weeping in 1 patient, respectively. Within the sham group 8 patients reported minor side effects, which included transient headache or migraine in 7 patients, worsened neck pain in 3 patients, tingling sensations in 2 patients and dizziness in 1 patient. In all reported cases, symptom worsening subsided shortly after the respective treatment unit. Another 2 patients, one from each group, discontinued study participation in consequence of recurrent headache during treatment, but were free of headaches at both follow-up assessments.

DISCUSSION

Summary of evidence

The present study is the first longitudinal randomized controlled trial that revealed efficacy for CST in comparison to manual sham treatment. In a patient sample with a mean duration of 9.6 years of non-specific neck pain, significant and clinically relevant effects on pain intensity were found directly after the active treatment period as well as at week 20, a further 3 months later. Minimal clinically important differences in pain intensity at week 20 were reported by almost 78% of the CST patients, while 48% even had substantial clinical benefit. Exploratory analysis revealed significant differences at week 20 also for pain on movement, functional disability, physical quality of life and patients' global impression of improvement. Pressure pain sensitivity and

body awareness were significantly improved only directly after the 8 weeks of treatment; anxiety only at week 20. No serious adverse events were reported.

Results are in line with previous pain research in CST and recommended neck pain treatments. While CST was shown to be effective in improving pain intensity, functional disability and health-related quality of life in comparison to waiting list,[52] relaxation[53,54], off-state physical devices[55,56] or standard medical care,[57] this study found comparable effects in blinded patients with respect to sham. Revealed effect sizes are comparable to those of neck pain guideline treatments[58-61] and more than likely cannot be explained exclusively by non-specific treatment effects, which were found to be only of small to medium effect sizes.[62] Specific effects of the used CST techniques appear to be probable, given fasciae' broad nociceptive and low-threshold mechanosensory innervation,[16,63] Treating fasciae has been shown to induce decreased tone of intrafascial muscle cells, decreased muscles tension, and increased parasympathetic nervous system response and vagal tone, in vitro[63] as well as in vivo.[64] Pain relief, decreasing muscles tension and the experience of deep relaxation and release were also reported by interviewed patients treated with CST.[65,66] Further described results of CST included the reduction of state and trait anxiety, whereas depression levels often were not significantly influenced.[29,56] Adverse events have been reported only by one randomized controlled trial in detail, with temporarily increased symptoms and tiredness occurring most often.[57] In CST theory, such transient symptom aggravation, tiredness and described emotional release reactions are usually understood as positive vegetative responses to treatment,[28] which were also reported in studies of osteopathy, massage therapy and acupuncture.[67-69]

Strengths and weaknesses

The strengths of the study design included the random and concealed allocation procedure, the intention-to-treat analysis, the active attention- and touch-control condition, comparable concurrent treatments, and the successful blinding of patients[47] and outcome assessors.

However, there are certain limitations. First of all, sample size was relatively small and consisted of 81.5% of female patients, which may reduce representativity and generalizability of the results. Even so, conducted analyses had adequate statistical power suggesting comparable results even in greater samples. Epidemiological surveys otherwise show a generally higher neck pain prevalence in women,[1,3] which in turn would explain the greater percentage of interested women than men. Second, comparability of the CST and sham group may be limited due to the allocation to the therapists. While three therapists performed CST, only one therapist did sham treatment. However, secondary analyses have shown that the alliance to the assigned therapists did not

systematically affect study outcomes.[47] Nonetheless, the used treatment protocols just enable to draw conclusions about the effect of CST on subjective clinical outcomes. It remains unclear, whether CST techniques actually affect indicated fascial structures and joints and if so, whether these changes in turn would result in quantifiable physiological responses. The design therefore would have to include further objective physiological measures and an even more standardized application of fascial palpation techniques.

Conclusions

CST was shown to be specifically effective and safe in reducing neck pain intensity and may improve functional disability and quality of life up to 3 months post intervention. Particularly in chronic and recurrent neck pain, CST may be a worthwhile treatment option in addition to standard medical care. Further studies with strict methodological designs and long-term follow-ups are needed to confirm CST efficacy in neck pain treatment.

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FIGURE LEGENTS

FIGURE 1. Consort flow chart of patient recruitment and loss.

FIGURE 2. Concurrent analgesics use (mean ± SD) of CST (black) and sham patients (grey) during the active study period.

TABLES

TABLE 1. Drop-out analysis.

	Completed week 8 (n=51)	Lost to week 8 (n=3)	P	Completed week 20 (n=45)	Lost to week 20 (n=9)	P
Age (years) (mean ± SD)	44.8±10.1	40.3±8.3	.455	44.7±10.4	44.3±8.7	.920
Gender (female|male) (%)	80.4|19.6	100|0	.390	79.5|20.5	90.0|10.0	.442
Education (<high school|high school|university degree) (%)	34.0|34.0|32.0	33.3|66.7|0	.553	29.5|34.1|36.4	55.6|44.4|0	.143
Employment (unemployed|employed|pensioned) (%)	3.9|92.2|3.9	0|100|0	.881	4.5|93.2|2.3	0|90.0|10.0	.411
Duration of pain (years) (mean ± SD)	9.9±9.1	4.6±4.6	.328	9.5±9.0	10.0±9.3	.889
Pain intensity at baseline (VAS) (mean ± SD)	64.5±13.2	60.0±0.66	.560	64.4±13.5	63.8±10.6	.898
Functional disability at baseline (NDI) (mean ± SD)	31.0±8.0	29.0±2.6	.672	31.3±7.6	28.8±8.6	.356
Treatment expectancy (CEQ) (mean ± SD)	6.8±1.3	6.7±1.2	.878	6.8±1.3	6.7±1.4	.833

CEQ, Credibility/Expectancy Questionnaire; NDI, Neck Disability Index; VAS, Visual Analogue Scale.

TABLE 2. Sample characteristics at baseline.

		Craniosacral		
	Total (n=54)	**Therapy (n=27)**	**Sham (n=27)**	**P**
Social demographics				
Age (years) (mean ± SD)	44.6±10.0	44.2±9.7	45.0±10.5	.769
Gender (female|male) (%)	81.5|18.5	70.4|29.6	92.6|7.4	.076
BMI (kg/m^2) (mean ± SD)	25.0±4.6	24.5±4.3	25.5±5.0	.461
Education (<high school|high school|university degree) (%)	34.0|35.8|30.2	33.3|29.6|37.1	34.6|42.3|23.1	.153
Employment (unemployed|employed|pensioned) (%)	3.7|92.6|3.7	7.4|88.9|3.7	0|96.3|3.7	.388
Neck pain characteristics				
Duration of pain (years) (mean ± SD)	9.6±8.9	9.9±9.2	9.3±8.8	.809
Pain intensity (VAS) (mean ± SD)	64.3±12.9	64.1±12.8	64.4±13.3	.942
Functional disability (NDI) (mean ± SD)	30.9±7.8	32.4±7.2	29.3±8.2	.140
Current pain medication (regularly|when needed) (%)	1.9|39.6	0|25.9	3.9|53.9	.052
Treatment history (%)				
Pain medication	59.3	48.2	70.4	.166
Injections	42.6	44.4	40.7	.783
Physical therapy	61.1	55.6	66.7	.577
Massage	75.9	74.1	77.8	.750
Acupuncture	31.5	29.6	33.3	.770
Chiropractic	33.3	29.6	37.0	.773
Relaxation techniques	27.8	29.6	25.9	.761
Psychotherapy	9.3	7.4	11.1	.639
Treatment expectancy (CEQ) (mean ± SD)	6.8±1.3	7.0±1.1	6.5±1.4	.136

CEQ, Credibility/Expectancy Questionnaire; NDI, Neck Disability Index; VAS, Visual Analogue Scale.

TABLE 3. Effects (mean ± SD) of Craniosacral Therapy in comparison to sham.

	Craniosacral Therapy (n=27)			Sham (n=27)			Between-group difference (95% CI)		P		Effect size (95% CI)	
	Baseline	Week 8	Week 20	Baseline	Week 8	Week 20	Week 8	Week 20	Week 8	Week 20	Week 8	Week 20
Pain												
Pain intensity (VAS)	64.1±12.8	31.7±20.7	31.6±19.0	64.4±13.3	53.5±20.3	47.8±19.3	-21.0 (-32.6|-9.4)	-16.8 (-27.5|-6.1)	.001*	.003*	1.02 (0.46|1.59)	0.88 (0.32|1.44)
Pain on movement (POM)	54.6±19.8	25.8±19.5	23.4±15.7	58.0±17.7	46.8±21.0	36.9±18.9	-18.6 (-29.2|-8.0)	-11.4 (-20.9|-1.9)	.001*	.020*	0.92 (0.36|1.48)	0.66 (0.11|1.21)
Point of max. pain (PPT)	234.4±120.1	255.4±122.9	226.5±62.6	238.5±137.1	206.7±77.1	204.9±63.4	50.3 (2.8|97.7)	23.9 (-9.9|57.3)	.038*	.163	0.52 (0.02|1.06)	0.38 (-0.16|0.91)
M. levator scapulae (PPT)	271.4±109.4	290.9±87.0	254.6±62.8	250.5±115.4	246.2±85.5	241.2±70.0	34.2 (-2.9|71.3)	10.4 (-25.1|45.8)	.070	.560	0.40 (-0.14|0.94)	0.16 (-0.38|0.69)
M. trapezius (PPT)	241.7±101.7	238.9±77.6	230.4±59.3	220.6±108.1	200.8±69.2	222.0±74.3	31.8 (-1.2|62.4)	4.4 (-28.9|37.7)	.042*	.788	0.43 (0.11|0.97)	0.07 (-0.47|0.60)
M. semispinalis capitis (PPT)	156.4±60.1	164.2±48.8	167.2±58.2	162.6±78.7	160.9±76.5	155.6±50.8	5.8 (-19.2|30.8)	15.1 (-12.4|42.5)	.644	.276	0.09 (-0.44|0.62)	0.28 (-0.26|0.81)

Physical health												
Functional disability (NDI)	32.4±7.2	17.6±11.6	18.5±7.5	29.3±8.1	24.8±10.8	23.9±8.7	-8.2 (-14.4|-2.1)	-6.5 (-11.1|-2.0)	.010*	.006*	0.73 (0.18|1.28)	0.80 (0.25|1.36)
Physical quality of life (SF-12)	38.0±8.3	47.2±9.0	48.5±5.1	41.2±6.0	43.3±9.3	43.2±5.9	5.8 (1.3|10.4)	5.9 (2.8|9.1)	.013*	.000*	0.64 (0.09|1.18)	1.07 (0.05|1.64)
Physical well-being (FEW)	2.9±0.6	3.1±0.8	3.1±0.6	2.7±0.8	2.7±0.8	2.8±0.8	0.2 (-0.2|0.5)	0.2 (-0.1|0.7)	.384	.155	0.19 (-0.34|0.72)	0.38 (-0.16|0.92)
Mental health												
Mental quality of life (SF-12)	48.5±10.6	51.2±9.7	48.4±10.0	48.8±11.4	47.7±12.5	46.2±12.4	3.5 (-1.6|8.5)	2.7 (-3.2|8.6)	.178	.363	0.31 (-0.23|0.85)	0.24 (-0.30|0.77)
Anxiety (HADS)	7.0±3.7	5.4±4.3	5.1±3.4	6.0±3.4	5.9±3.6	6.7±3.8	-1.0 (-2.8|0.9)	-2.1 (-3.8|-0.3)	.299	.020*	0.24 (-0.30|0.78)	0.58 (0.03|1.12)
Depression (HADS)	4.8±3.5	4.1±4.0	5.0±3.5	4.4±3.5	4.7±3.7	6.8±3.8	-0.7 (-2.2|0.8)	-1.9 (-3.9|0.2)	.329	.079	0.19 (-0.35|0.72)	0.50 (-0.04|1.05)
Stress perception (PSQ)	44.9±14.6	40.8±18.0	38.7±15.5	47.6±18.5	45.2±20.3	47.2±19.9	-0.4 (-3.2|7.4)	-6.4 (-15.5|2.8)	.912	.171	0.02 (-0.51|0.56)	0.36 (-0.18|0.89)
Pain acceptance	2.8±0.5	3.0±0.7	3.2±0.6	3.0±0.5	3.0±0.4	3.0±0.5	0.1 (-0.2|0.4)	0.2 (-0.1|0.4)	.392	.146	0.21 (-0.33|0.74)	0.37 (-0.17|0.91)

(ERDA)												
Body connection												
Body awareness (SBC)	2.9±0.5	3.1±0.5	3.1±0.5	2.8±0.6	2.7±0.6	3.0±0.5	0.3 (-0.1|0.5)	0.1 (-0.1|0.4)	.001*	.330	0.59 (0.04|1.13)	0.26 (-0.27|0.80)
Body dissociation (SBC)	0.8±0.4	0.8±0.7	0.9±0.4	0.7±0.6	0.7±0.5	0.8±0.8	0.9 (-0.1|0.4)	0 (-0.3|0.3)	.183	.935	0.30 (-0.23|0.84)	0.02 (-0.51|0.55)
Global improvement												
Global improvement (PGI-I)	−	2.2±1.0	2.3±1.1	−	3.3±1.0	3.1±1.1	-1.0 (-1.5|-0.5)	-0.7 (-1.3|-0.1)	.000*	.029*	1.01 (0.45|1.58)	0.62 (0.07|1.17)

CEQ, Credibility/Expectancy Questionnaire; CI, confidence interval; ERDA, Emotional/Rational Disease Acceptance Questionnaire; FEW, Questionnaire for Assessing Subjective Physical Well-being; HADS, Hospital Anxiety and Depression Scale; NDI, Neck Disability Index; PGI-I, Patients' Global Impression of Improvement; POM, Pain on Movement Questionnaire; PPT, pressure pain thresholds; PSQ, Perceived Stress Questionnaire; SBC, Scale of Body Connection; SF-12, 12-item Short Form Health Survey; VAS, Visual Analogue Scale; *, significant between-group difference (p≤.05).

TABLE 4. Responder analysis.

	Craniosacral Therapy (n=27)		**Sham (n=27)**		
	Non-responder	**Responder**	**Non-responder**	**Responder**	**P**
20% VAS reduction at week 8	7 (25.9%)	20 (74.1%)	16 (59.3%)	11 (40.7%)	.013*
20% VAS reduction at week 20	6 (22.2%)	21 (77.8%)	13 (48.1%)	14 (51.9%)	.046*
50% VAS reduction at week 8	15 (55.6%)	12 (44.4%)	23 (85.2%)	4 (14.8%)	.017*
50% VAS reduction at week 20	14 (51.9%)	13 (48.1%)	20 (74.1%)	7 (25.9%)	.091

VAS, Visual Analogue Scale; %, within-group percentages; *, significant between-group difference (p≤.05)

Figure
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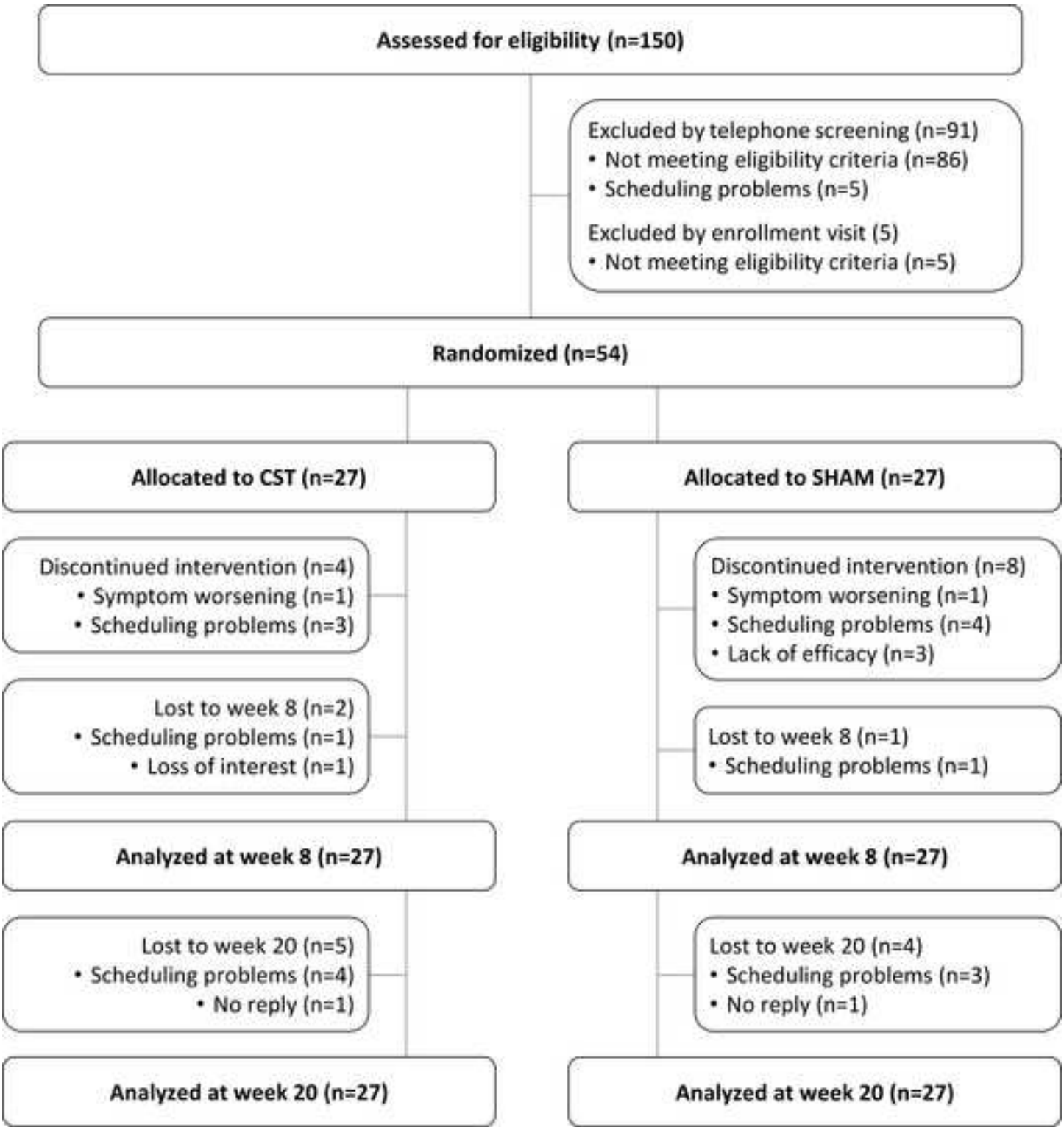

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