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Somatosensory rehabilitation for allodynia in complex regional pain syndrome of the upper limb: A retrospective cohort study



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ABSTRACT

Study Design: Retrospective cohort study.

Introduction: Somatosensory rehabilitation is a standardized method of evaluation and conservative treatment of painful disorders of vibrotactile sensation, including the mechanical allodynia and burning pain of complex regional pain syndrome (CRPS).

Purpose of the Study: The purpose of this study was to examine the effectiveness of somatosensory rehabilitation for reducing allodynia in persons with CRPS of 1 upper limb in a retrospective consecutive cohort of patients.

Methods: An independent chart review of all client records (May 2004–August 2015) in the Somatosensory Rehabilitation Centre (Fribourg, Switzerland) identified 48 persons meeting the Budapest criteria for CRPS of 1 limb who had undergone assessment and treatment. Outcomes of interest were the French version of the McGill Pain Questionnaire (Questionnaire de la Douleur St-Antoine [QDSA]), total area of allodynia as recorded by mapping the area of skin where a 15-g monofilament was perceived as painful, and the allodynia threshold (minimum pressure required to elicit pain within the allodynic territory).

Results: This cohort was primarily women (70%), with a mean age of 45 years (range: 18–74). Mean duration of burning pain was 31 months (range: 1 week–27.5 years), and baseline QDSA core was 48. The average primary area of allodynia was 66 cm² (range: 2.6–320), and the most common allodynia threshold was 4.0 g. The average duration of treatment was 81 days. At cessation of treatment, the average QDSA score was 20 (effect size Cohen's $d = 1.64$). Allodynia completely resolved in 27 persons (56% of the total sample where only 58% completed treatment).

Discussion: This uncontrolled retrospective study suggests that somatosensory rehabilitation may be an effective treatment with a large effect size for reducing the allodynia and painful sensations associated with CRPS of the upper limb. More work is in progress to provide estimates of reliability and validity for the measurement tools for allodynia employed by this method.

Level of Evidence: 2c.

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Introduction

Complex regional pain syndrome (CRPS) is a neuropathic pain condition; it typically presents with autonomic and inflammatory symptoms accompanying burning pain and sensitivity in a limb.^{1,2} Although there is no defining diagnostic test for CRPS, clinical diagnostic criteria are used to assist in the differentiation of the symptoms from the normal sequelae of trauma or nerve injury.^{2,3}

Although it is often associated with an acute injury, it can become chronic in nature.^{4,5} Factors associated with poor prognosis include somatosensory changes such as burning pain and allodynia^{6,7} as well as motor symptoms such as persistent stiffness and contracture.^{5,7} Severe allodynia has been associated with poor response to medical interventions⁸ and is a pragmatic barrier to participation in traditional rehabilitation programs. Although physiotherapy and occupational therapy are considered the foundation for management of CRPS,^{9–11} there is a need for more evidence-based rehabilitation interventions.^{12–14}

Somatosensory rehabilitation is an umbrella term for a standardized method of evaluation and conservative treatment of painful disorders of cutaneous vibrotactile sensation, including mechanical allodynia with or without spontaneous neuropathic pain, as well as the burning or “boiling” pain of CRPS.¹⁵ The theoretical basis is 2-fold: neuropathic pain by definition originates from some form of lesion in the nervous system¹⁶ and somatosensory alterations, including both tactile hypoesthesia and mechanical allodynia, cause pain. Altered somatosensory perception of all signals from this area as pain can be explained by peripheral sensitization and/or central sensitization.^{17–19} First proposed over 16 years ago, the key tenets in somatosensory rehabilitation for the identification and treatment of static mechanical allodynia include:

- precise psychophysical evaluation of the skin using a 15-g monofilament to define the territory that is painful to touch;
- formation of an anatomical hypothesis of the peripheral nerve branch(es) underlying the painful territory and contributing to the aberrant afferent pain signalling and perception;
- avoiding reinforcement of the sensitization mechanisms by minimizing evocation of pain by temporarily limiting touch (and consequently functional use) of the painful zone; and
- comfortable somatosensory “counter stimulation” (tactile and/or vibratory) on an anatomically related cutaneous branch (a proximal cutaneous area of the same branch or arising from the same cord of the brachial plexus).¹⁵

Although the clinical application of somatosensory rehabilitation method (SRM) has been well described in non-peer-reviewed literature,^{15,20} to date, there have only been a few peer-reviewed articles focusing on the effectiveness of the technique with specific populations, addressing both allodynia and hypoesthesia across a spectrum of nerve lesions.^{21–23} Given the need for clinical modalities to address the allodynia that limits both activities of daily living and participation in rehabilitation for persons with CRPS, this study will seek to evaluate the clinical results of the SRM for this population.

Purpose of the study

Our primary objective was to answer the research question: How effective is somatosensory rehabilitation for allodynia in persons with CRPS of 1 upper limb? However, given this is a novel treatment method, our secondary objective was to explore the theoretical constructs and hypothetical relationships underpinning the method.

Methods

Design and setting

This retrospective study was based on a chart review conducted at a single center (the Somatosensory Rehabilitation Centre) in Fribourg, Switzerland, by an independent investigator (T.P.). All files of clients who were no longer receiving treatment at the center were reviewed, from its opening in July 2004 to August 2015. Clients were referred by a medical doctor, and assessments and

treatments followed a detailed clinical protocol (described in the following section). Clients attended a weekly treatment session and were seen on alternate weeks by two occupational therapists trained in the SRM.¹⁵ In this time frame, 14 different therapists were employed at the Somatosensory Rehabilitation Centre and contributed to the client records included in this study.

Subjects

All consecutive patient records identified as (1) meeting the Budapest criteria for CRPS²⁴ and (2) demonstrating static mechanical allodynia (defined as a painful response to stimulation with a 15-g monofilament) were included in this retrospective cohort, regardless of whether they attended or completed treatment. Persons identified as having CRPS who demonstrated tactile hypoesthesia but no allodynia was not included, as our focus was on allodynia. It is important to note all patients reporting spontaneous neuropathic limb pain are systematically screened using the Budapest criteria as a checklist as part of the initial evaluation at the Somatosensory Rehabilitation Centre, and these results were clearly documented in clinic files.

Outcome measures

The primary outcome measure was the French version of the McGill Pain Questionnaire (QDSA [Questionnaire de la Douleur St-Antoine])²⁵; however, if the subject was unable to complete this assessment because of language barriers, other validated translations of the McGill were used. The QDSA is comprised of 58 pain descriptors, with sensory (35 word) and affective (23 word) subscales; words are further arranged in construct clusters (temporal, spatial, thermal, and so forth).²⁵ The subject is instructed to first choose all words that describe their current pain (yielding a total number of words/58). From these chosen words, the “best” word from each cluster is rated using a 0–4 scale (0 = absent, 1 = mild, 2 = moderate, 3 = strong, and 4 = very strong) to indicate the severity of this pain at the present time. These ratings are summed and converted to z scores for ease of interpretation, yielding a total score tQDSA/100, as well as sensory pain score (sQDSA)/100, and affective pain score (aQDSA)/100.

In the SRM, allodynia is quantified in 2 ways: allodyniography and the rainbow pain scale.^{15,21} Allodyniography is a mapping technique using a standard 15-g stimulus (Semmes-Weinstein monofilament: mark 5.18) to outline the borders of the territory where application of the stimulus to the skin produces pain (30 mm on a 100-mm visual analogue scale [VAS], or pain at rest + 10 mm on a 100-mm VAS).²¹ The territory of the allodyniography is recorded visually on graph paper: see the study by Spicher et al,²¹ for a detailed description of the technique. However, the mathematical area of the territory can also be estimated from measurements taken relative to invariant anatomical reference points. To account for the reality of a nonrectangular shape of the allodynic territory, we calculated the area of the allodynia as length (most proximal and distal points identified) × width (most lateral points identified) × 0.66; see [Figure 1](#) for an illustrative example. The rainbow pain scale is a categorical scale rating the severity of the allodynia within the allodynic territory. This is tested with vision occluded by touching the center of the painful area with a series of monofilaments. Starting with the smallest pressure (0.04 g/2.83 log), a single stimulus is applied for 2 seconds with each monofilament (with a 10-second interval between applications), progressing to greater pressure categories (see [Figure 2](#)) until the subject indicates that the stimulus has become painful (30 mm on 100 mm visual analogue scale [VAS], or pain at rest + 10 mm on a 100-mm VAS). As soon as a stimulus is painful, the testing is

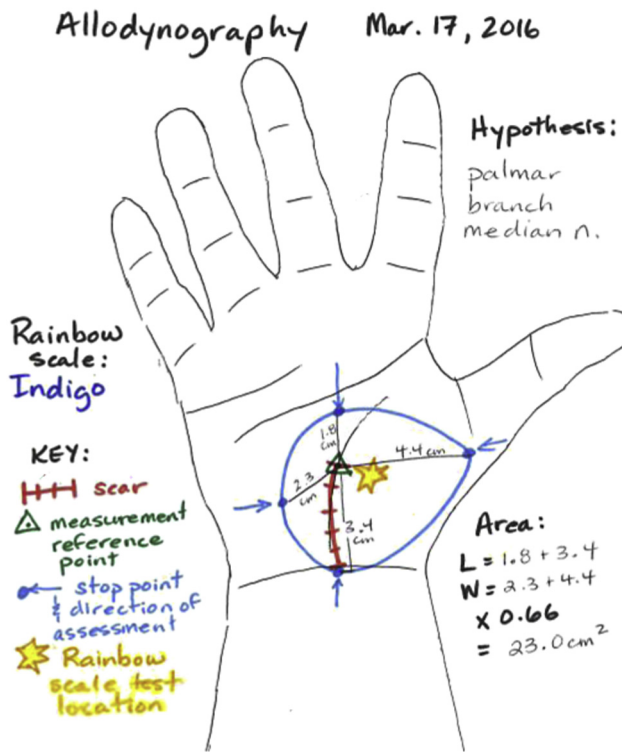


Fig. 1. Sample allodynia map. (1) Hypothesis designates the cutaneous nerve branch related to the mapped territory. (2) Arrows indicate the direction of testing, while dot indicates where the subject indicated “STOP.” (3) Green triangle indicates invariant measurement reference point. (4) Star indicates the point where the rainbow scale was tested. (5) Rainbow scale indicates the severity of allodynia. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

discontinued, and the rainbow scale category is recorded as the first stimulus perceived as painful. To minimize the effects of summation,¹⁷ the rainbow scale evaluation is not completed at the same time as the allodyniography but is recorded at the next subsequent visit (typically 1 week later).¹⁵ Individual pressure categories in the rainbow scale have subsequently been clustered into descriptive groupings of discrete, consequential, and serious (see Fig. 2) based on observations in clinical practice but has not been studied.

In conjunction with the allodyniography, an anatomical hypothesis is formed to identify which cutaneous nerve branch is the primary supplier of the allodynic territory and therefore potentially the source of the nerve lesion generating the neuropathic pain.¹⁶ This hypothesis is recorded on the allodynia map and used to inform the treatment regime. On the initial visit, the primary allodyniography is recorded for only the most painful area. Although the client may have several areas of pain or may report

diffuse pain across an entire limb or hemisphere, they are asked to identify the most painful area. As treatment progresses, they may identify additional areas of allodynia, and secondary allodynia maps (and associated cutaneous branches) are recorded for those additional locations.

The assessment protocol was completed as follows: (1) QDSA and allodyniography at the first/baseline visit; (2) rainbow pain scale on first subsequent visit; (3) repeat evaluation of QDSA and allodyniography every 4 weeks, or sooner if indicated; and (4) esthesiography (mapping of the underlying area of tactile hypoesthesia)^{21,22} and quantitative somatosensory testing including static 2-point discrimination, vibration perception threshold, and pressure perception threshold when the allodyniography is negative (15 g stimulus to the skin is not perceived as painful) for 2 consecutive visits. The QDSA, static 2-point discrimination, vibration perception threshold, and pressure perception threshold were also recorded at discharge. For those clients not completing the recommended course of treatment, the reason for exiting treatment was recorded using the categories (1) lack of progress with current regime (patient perspective), (2) other life issues (ie, moved away and cost barriers), (3) other health issues, (4) did not ascribe to the treatment program/dropped out, (5) no further recovery expected (therapist perspective), or (6) returned to work and unable to continue attending.

Intervention

The treatment regime for the SRM has 3 core elements: distant vibrotactile counter stimulation (DVCS), application of therapeutic vibration, and avoidance of any touch stimuli that evoke pain. The first element is carried out as a home program where DVCS is applied 8 times daily for no longer than one minute; however, formal treatment diaries were not used to track adherence. DVCS uses the medium perceived by the client as the most comfortable version of light touch (typically rabbit fur or a plush microfleece), applied in a light stroking motion. It is not applied to the painful area; instead, it is applied to an area of the skin with normal sensation that is anatomically related to the sensitized cutaneous branch hypothesized to underlie the allodynic territory. For example, the sensitization hypothesis for the allodynic territory illustrated in Figure 1 is the palmar cutaneous branch of the median nerve. Therefore, DVCS would be applied to the cutaneous territory of a more proximal branch of the same nerve or any nerve joining the same cord of the brachial plexus. In this case, it would be the lateral antebrachial cutaneous nerve, which joins the median nerve in the lateral cord of the brachial plexus.²⁶ If this cutaneous area also demonstrated somatosensory abnormalities or stimulation in this area was not comfortable, then DVCS would be applied on the ipsilateral side in a dermatomal area above or below the nerve roots for the sensitized branch (ie, in the T1/T2 area just below the collarbone). Vibration stimulation was applied to the same area as DVCS for 10 minutes during weekly clinic visits, using the Vibradol (Rehaxone, Sierre, Switzerland). Finally, the occupational therapist reviewed activities of daily living with each individual client and collaboratively identified sources of evoked pain (such as the rubbing of clothing and tool use) and developed strategies to avoid stimulation and/or delegate provocative tasks until the resolution of the allodynia.

Statistical analysis

Primary objective

After screening for high/low values that might suggest data entry errors, descriptive statistics of demographics and continuous clinical variables were tabulated using means ± standard deviations (SDs) and frequencies/percentages for categorical variables. To address our primary question on effectiveness, QDSA total



Fig. 2. Rainbow pain scale. The colors represent the severity of allodynia as represented by the smallest amount of pressure which elicits a painful response. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

scores before and after treatment were compared using 2-sided paired sample Student *t*-tests, with 95% confidence intervals and estimates of effect size using Cohen's *d* (employing an on-line sample size calculator at http://www.psychometrica.de/effect_size.html#dep) to account for the paired or dependent sample.

Secondary objective

To explore and illustrate theoretical constructs within the SRM, we generated 8 a priori hypotheses (see Table 1).

For the regression analyses, normality of the distributions for each variable was assessed statistically and graphically. In multiple regression analysis, we also examined for collinearity using pairwise correlations and scatter plots. For all regression analyses, we followed the analysis with formal regression diagnostics: testing homogeneity of variances, calculating leverage and influence, testing the normality of the residuals, and plotting residuals against predicted values and leverage, and calculation of the variance inflation factor. To develop the ideal model for multiple linear regression, outliers with strong influence were removed, the regression model rerun, and the homogeneity of variances and normality assumptions were checked again. Differences between groups (single nerve lesion vs multiple, nerve lesion in hand vs arm vs trunk) were examined using analysis of variance, with dummy coding for categorical variables.

All analyses were performed with Stata 13, with statistical significance set at $P = .05$ unless otherwise noted.

Results

Subjects

Fourty-eight records were identified for persons demonstrating allodynia accompanying CRPS. About 70.4% were female, and the average age was 45 years. The average area of allodynia

was 65.7 cm² and of “discrete” severity¹⁵ (35.6% were categorized as purple or indigo on the rainbow scale; see Fig. 2). Psychological comorbidities reported included posttraumatic stress disorder ($n = 1$, 2.1% of subjects) and anxiety or depression in $n = 4$ or 8.4%; these were identified by the referring physician or reported by the client during the initial history taking. See Table 2 for a summary of demographics and clinical features. Twenty-two persons had evidence of a single nerve lesion in the upper extremity, whereas 26 persons presented with multiple nerve lesions. Thirty-one different cutaneous nerve branches were identified as underlying the allodynic areas, with the palmar branch of ulnar nerve ($n = 12$, 13.6%) and the palmar branch of median nerve ($n = 11$, 12.5%) being the most common. Overall, more nerve lesions were seen in the hand (70.5% of identified branches) as compared with the arm (23.9%). The average reported duration of neuropathic pain symptoms (not time since CRPS diagnosis) was 31.2 months but ranged greatly from 1 month to over 25 years. Baseline QDSA total scores were also highly variable, ranging from 4 to 99 at baseline, with an average score of 48.1 ± 17.7 ; final scores averaged 20.1 ± 20.0 . However, it is worth noting that “baseline” for identification of the painful area/nerve lesion was not necessarily the first treatment visit for the person; in fact, all QDSA scores below 20 at “baseline” were related to secondary or tertiary lesions and did not represent the pain score on the subject's first visit.

Effectiveness of somatosensory rehabilitation

A paired sample *t*-test was conducted to compare QDSA total scores at baseline and final evaluations. There was a significant difference in the baseline tQDSA ($x = 51.4$, $SD = 17.4$) and final tQDSA ($x = 20.4$, $SD = 20.0$); $t(57) = 13.6$, $P < .001$. These results suggest that somatosensory rehabilitation treatment reduced self-reported pain qualities in this set of 48 patients with 88 nerve

Table 1
Construct questions and hypotheses

Question	Hypothesis	Variables	Statistical method
1 What is the nature and strength of the relationship between severity of pain and severity of mechanical allodynia at baseline?	There will be a weak positive relationship between these different constructs	QDSA Rainbow scale	Correlation and simple regression
2 What is the nature and strength of the relationship between duration of pain and area of allodynia at baseline?	There will be a weak positive relationship, reflecting the spread of chronic pain beyond the initial noxious event	Duration of NeP Mathematical area of allodynic territory	Correlation and simple regression
3 Is there a difference in duration of pain between different levels of allodynia (severity) at baseline?	There will be a significant positive relationship, with increasing duration seen with increased severity	Duration of NeP Rainbow scale	ANOVA
4 What is the nature and strength of the relationship between the area of allodynia and severity of allodynia at baseline?	There will be a weak positive relationship, as they are unique constructs	Area of allodynia Rainbow scale	Correlation and simple regression
5 Does the severity of allodynia at baseline predict the duration of treatment required to resolve it?	There will be a strong relationship between severity and duration of treatment	Rainbow scale Duration of DVCS	Correlation and simple regression
6 What factors predict change in QDSA scores?	Change in QDSA scores will be multifactorial	QDSA change, age, rainbow scale, gender, duration of NeP, nerve lesion location, area of allodynic territory, and # of nerve lesions	Stepwise multiple regression
7 Do persons with a single nerve lesion report less pain than persons with evidence of multiple lesions?	Persons with multiple lesions will report more pain	# of nerve lesions (coded as single or multiple) and QDSA	ANOVA
8 Do persons with a single-nerve lesion in the hand (where there is a higher density of nerve endings) report more pain than persons with a single-nerve lesion in the arm or trunk?	Persons with lesions in the hand will report more pain than those with more proximal lesions because of the higher density of nerve endings	Nerve lesion location (coded as hand, arm, or trunk), QDSA	ANOVA

ANOVA = analysis of variance; DVCS = distant vibrotactile counterstimulation; QDSA = Questionnaire Douleur St. Antoine; NeP = neuropathic pain; # = number.

Table 2
Demographics and clinical features, $n = 48$ persons

Demographics and clinical features	Mean	Standard deviation	Range
Age (in y)	45.4	13.4	18–74
Duration of NeP (in mo)	31.2	57.5	1–335
Baseline tQDSA (in points)	48.1	17.7	5–99
Final tQDSA score (in points)	20.1	20.0	0–75
Area of allodynia (in cm ²)	65.7	78.6	2.6–320.8
Duration of DVCS (in days)	81.0	76.4	5–381
Demographics and clinical features	Frequency	Percentage	
Gender	Females = 34	70.4	
	Males = 14	29.6	
Rainbow Pain Scale ($n = 59$ allodynic lesions)	Violet = 12	20.3	
	Indigo = 9	15.3	
	Blue = 12	20.3	
	Green = 7	11.9	
	Yellow = 10	17.0	
	Orange = 1	1.7	
	Red = 8	13.6	
Cutaneous branch injured or damaged ($n = 88$) ^a (5 most frequently reported are recorded here)	Palmar branch of ulnar nerve	13.6	
	Palmar branch of median nerve	12.5	
	Dorsal branch of ulnar nerve	9.1	
	Superficial branch of radial nerve	8.0	
	Superior lateral cutaneous nerve of arm	8.0	
Nerve lesion region ($n = 88$) ^a	Hand = 62	70.5	
	Arm = 21	23.9	
	Thoracic = 5	5.7	
Reason for exiting treatment ($n = 88$: recorded for lesion, not for subject) ^a	Lack of progress = 3	3.4	
	Other life issues = 4	4.6	
	Other health issues = 4	4.6	
	Dropped out = 9	10.2	
	No progress expected = 2	2.3	
	Completed treatment = 51	58.0	
	Not determined = 15	17.1	

DVCS = distant vibrotactile counter stimulation; NeP = neuropathic pain.

^a Please note: 26 subjects had multiple lesions identified, with a total number of lesions $n = 88$; of these 88 lesions, each person had at least 1 lesion meeting the criteria for allodynia, with a total # of allodynic lesions, $n = 59$).

lesions. Effect size was calculated at Cohen's $d = 1.64$, using a formula which accounted for the inherent correlation of our paired samples. Of this cohort, reasons for ceasing treatment at final evaluation were reported, with 58% (51/88 lesions) having completed their treatment, 10.2% dropping out of treatment (i.e. not attending booked follow-up), 3% ceasing treatment because the

patient did not see any change (ie declining to book follow-up), 2% ceasing because the therapist did not feel it was beneficial, and 10% ceasing treatment because of work, health, or life issues. Final tQDSA scores were also calculated for the subgroup identified as completing a full course of treatment; these demonstrated lower mean scores ($x = 12.3$, $SD = 10.2$, range: 0–41).

Table 3
Summary of results for secondary analyses

Question/relationship investigated	Results			Significance
	N	Coefficients	Meets statistical assumptions	
1 Severity of pain and severity of mechanical allodynia at baseline?	54	$R^2 = 0.0004$ $F[1,52] = 0.02$	✓	.88
2 Duration of pain and area of allodynia at baseline?	32	$r = 0.037$ $R^2 = 0.05$ $F[1,30] = 1.43$	✓	.24
3 Duration of pain between different levels of allodynia (severity) at baseline?	61	$F[1, 60] = 2.08$ $R^2 = 0.22$	✓	.06
4 Area of allodynia and severity of allodynia at baseline?	32	$R^2 = 0.17$ $F[1,30] = 6.17$	✓	.02
5 Severity of allodynia at baseline predicting the duration of treatment required to resolve it?	36	$R^2 = 0.23$ $\beta_0 = 2.55$ $\beta_1 = 0.88$	✓	.003
6 Prediction of change in QDSA scores?	17	$R^2 = 0.35$ $F[1,15] = 8.01$	✓	.01
6b Gender differences in change in QDSA scores?	58	$F[1,56] = 5.88$ $R^2 = 0.10$	✓	.02
7 Pain level and number of nerve lesions (single vs multiple)?	76	$F[1,74] = 4.65$	✓	.03
7b Pain level and single vs multiple lesions and duration of NeP	75	Model $R^2 = 0.10$ β_1 # of nerve lesions β_2 NeP duration	✓	.03 .95
8 Pain level and location of lesion (hand vs arm vs trunk)?	76	$F[2,73] = 3.72$	✓	.03

Bold values indicate statistical significance $<.05$.

Relationships of clinical characteristics, pain, and treatment response

Refer to Table 3 for a summary of results of secondary analyses.

Linear regression was used to investigate the relationship at baseline between the tQDSA and severity of mechanical allodynia as measured by the rainbow scale. There were 54 data sets with this information used for this analysis. The severity of mechanical allodynia required transformation by calculating the square root of each value to normalize the data distribution prior to analysis. This model generated $R^2 = 0.0004$, $P = .88$; $F[1,52] = 0.02$. Post hoc analyses confirmed the homogeneity of variance and normal distribution of the residuals. This suggests that there is only a weak correlation between the variables and that the severity of allodynia did not explain any of the variance in QDSA values at baseline. We then looked to see if there was a correlation between the duration of neuropathic pain at baseline and the (adjusted) area of allodynia. Pearson's correlation was small at $r = 0.037$ using the 32 available data sets; further examination of this relationship using transformed data to normalize the distribution (logarithmic transformation applied) was also nonsignificant at $R^2 = 0.0455$, $P = .24$; $F[1,30] = 1.43$. Post hoc tests confirmed the assumptions of regression, meaning we can be confident in the model suggesting there is only a weak correlation between duration of neuropathic pain and the size of the area of allodynia, and the duration of pain did not predict the variability seen in the area of allodynia.

We were also interested in whether the severity of allodynia was influenced by the duration of neuropathic pain. Analysis of variance was therefore conducted to examine whether average duration of pain (transformed logarithmically to normalize the distribution) differed across categories of allodynia severity; this was again nonsignificant at $F[1, 60] = 2.08$, $P = .06$ based on analysis of 61 available data sets. We then progressed to look at if there was a relationship between the size of the area of allodynia and the severity of allodynia within that territory. Regression analysis of the transformed variables (log transformation of area; squaring of rainbow pain scale values) suggested a small but significant relationship existed, at $R^2 = 0.1706$, $P = .02$, $F[1,30] = 6.17$. Post hoc analyses again confirmed the homogeneity of variance and normal distribution of residuals. Conversion back from the transformed values to the original units of measurement suggests on average, the adjusted area of allodynia increases by 1.25 cm^2 for every increase in the Rainbow Pain Scale severity.

Regression analysis was used to explore the relationship between the severity of allodynia at baseline, and the duration of distant vibrotactile counter stimulation required to see it resolve. Analysis was based on 36 cases with this data available; however, both variables needed transformation to normalize their distribution (using the square root of allodynia severity values and the log of duration of DVCS values). This generated $R^2 = 0.23$, $P = .003$; $\beta_0 = 2.55$, $\beta_1 = 0.88$ and met the requisite assumptions of heteroskedasticity and normality of the distribution of the residuals. After conversion of the beta coefficients back to the original units, this suggests for every increase in the severity of allodynia, the duration of DVCS necessary to resolve it increases by 24.4 days. Post hoc power analysis supported this analysis was fully powered to find this relationship; however, it should be noted that severity of allodynia only explained 23% of the variation seen in the duration of DVCS required.

We conducted stepwise regression to see what factors would predict change in QDSA scores from baseline to final evaluation (dependant variable). The independent variables of age, gender, nerve lesion location, rainbow scale, area of allodynic territory, number of nerve lesions, and duration of neuropathic pain were introduced into the model (after transformation to normalize

distribution if required). Variables were retained if they had a statistical significance of less than $P = .05$ and were removed if significance was greater than $.06$. This only retained gender in the final model $R^2 = 0.35$, $P = .01$, $F[1,15] = 8.01$; the coefficients suggested that women saw greater reductions in pain than men. Analysis of variance was therefore conducted to look at the difference in change in QDSA scores and gender. Again, there was a significant effect of gender on change in QDSA scores ($F[1,56] = 5.88$, $P = .02$) with a larger sample of $n = 58$ observations; the mean difference in QDSA change scores between men and women was 12.4 points, with women achieving greater change in score. However, it is also important to note that based on the R^2 value ($R^2 = 0.10$), gender only explained 10% of the variance.

Analysis of variance was conducted to examine for differences in baseline QDSA scores between persons with a single nerve lesion ($n = 22$) or those with multiple nerve lesions ($n = 26$). There was a significant effect of the number of nerve lesions on the QDSA total scores ($F[1,74] = 4.65$, $P = .034$). The average QDSA score for persons with a single nerve lesion was 55.5, whereas the mean QDSA score for persons with multiple nerve lesions was 45.6, suggesting that persons with multiple nerve lesions reported less pain than those with a single nerve lesion. This unexpected finding raised the question if the incidence of multiple lesions was related to a longer duration of pain. To explore this hypothesis, we conducted a regression analysis of baseline QDSA scores and introduced the 2 dependent variables of number of nerve lesions (categorized as single or multiple) and duration of neuropathic pain (NeP) (with score conversion to log values for normalizing the distribution). This model confirmed a significant effect of number of nerve lesions but including the duration of NeP did not explain any additional variance ($R^2 = 0.10$, $P = .03$ for the total model; but $P = .95$ for the β_2 value of NeP duration; the β_1 for number of nerve lesions was significant at $P = .007$). Post hoc analysis confirmed that this model met the regression requirements for homogeneity of variances ($P = .21$, so actual variance was not different than predicted) and normal distribution of residuals ($P = .38$ is not different from the normal distribution). This means that we can be confident in our findings that having more than one nerve lesion predicts a lower QDSA score at baseline but only explains 10% of the variance seen in those scores.

Analysis of variance was also conducted to see if there was a difference in baseline QDSA scores between subjects with nerve lesions in their hand and those with nerve lesions in the forearm/arm or trunk. There was a significant effect of the location of the nerve lesion on baseline QDSA total for the 3 locations ($F[2,73] = 3.72$, $P = .03$). The mean QDSA total score for nerve lesions of the hand was 45.7, for the arm was 57.7, and for lesions on the trunk was 40.2. Post hoc testing with Bonferroni correction for multiple comparisons shows that the significant differences lie between nerve lesions in the hand compared with the arm ($F[1,73] = 6.31$, $P = .03$), whereas no differences were found between the scores for nerve lesions in the hand vs the trunk ($F[1,73] = 0.48$, $P = .98$) and nerve lesions in the trunk compared with the arm ($F[1,73] = 4.04$, $P = .10$). Given the mean score for lesions on the trunk is the lowest of the 3 mean scores and the mean score for lesions on the arm is the highest, it is counter intuitive that no difference would be found when comparing the trunk to the arm; however, due to the high level of variability in the trunk scores, the 95% CI when comparing those 2 values was very large and included 0. Thus nerve lesions of the forearm and arm were reported as statistically significantly more painful than nerve lesions in the hand.

Discussion

This retrospective, uncontrolled cohort study has generated preliminary evidence for the effectiveness of the SRM and some

hypothesized relationships of the supporting constructs. There is a need for mechanism-specific¹⁸ rehabilitation interventions for CRPS to address the burden of pain^{27,28} and the impact on daily activities.²⁹ Somatosensory rehabilitation is a method of assessment and treatment specifically intended to address the sensory aspects of neuropathic pain, including the allodynia frequently seen in CRPS.¹⁵ The theoretical mechanism for the effect of the SRM is the reduction of central sensitization by addressing the altered peripheral signaling. This mirrors the work of others who have demonstrated reduction in pain syndromes with features of central sensitization (such as phantom limb pain) by addressing peripheral pain generators.^{30–32}

The treatment target of somatosensory rehabilitation is the skin²¹ and its rich network of cutaneous nerve endings as the entry point to the nervous system.³³ Furthermore, the skin itself has the ability to produce neurotransmitters and peptides such as serotonin and cortisol, and tactile stimulation can drive the local immune and inflammation regulatory responses.^{34,35} Somatosensory rehabilitation seeks to apply comfortable sensory stimulation to a cutaneous nerve branch anatomically related to the peripheral lesion,¹⁵ where the neurotransmitters generated from this comfortable stimulation have the opportunity to reduce the aberrant signaling.³² This represents a distinct departure from traditional “desensitization” interventions,^{2,36,37} which seek to flood the area of altered sensation with intense sensory stimuli, with the intent of producing “...sensory accommodation to the stimulus”(p.1715).³⁸ However, the term “tactile desensitization” has also been used to describe sensory motor reeducation programs for CRPS³⁹ using conscious attention to direct stimulation of the painful area.^{39,40} In contrast, the SRM seeks to avoid all tactile stimulation to the painful area and focuses on stimulation to related areas of normal sensation to resolve allodynia, followed by sensory reeducation to address the residual hypoesthesia after the allodynia has abated.²¹ This strategy of avoiding tactile stimuli recognizes that only low-level, nonnoxious stimuli are required to maintain the modulated neuroplasticity after nerve lesion⁴¹ and that simply performing activities of daily living is sufficient to sustain central sensitization.⁴² Future work should explore the relative contributions of distant vibrotactile counterstimulation and avoidance of tactile stimulation (including the modification of daily activities) to the effectiveness of this treatment method for the reduction of allodynia.

This study describes the use of SRM for persons with CRPS of a single upper limb. These patients were identified using the Budapest clinical criteria²⁴ at baseline. However, this evaluation was not repeated at discharge or end of treatment, so it is not known if the subjects would have continued to meet the criteria after treatment. Our results demonstrate that few patients had zero pain at final evaluation (see Table 2); however, this aligns with the general literature on the outcomes of CRPS, which reports many people continue to experience pain, stiffness, and cold intolerance.^{4,5} Although patients exiting treatment may not have complete resolution of CRPS symptoms, it was often anticipated that they would be better able to participate in other forms of treatment like graded motor imagery⁴³ to address residual motor symptoms. In addition, this was reflective of a consecutive cohort where only 58% of participants completed treatment.

We conducted an intention to treat analysis, including any follow-up results available, regardless of if the person had completed the full course of treatment. Despite this, the effect size should be considered large at $d = 1.64$.⁴⁴ It is also worth noting that the average duration of neuropathic pain symptoms reported at baseline was more than 2 years; however, the duration of symptoms was not shown to be predictive of baseline pain or change in pain from baseline to final evaluation.

Nedelec et al²³ recently published their results using the SRM for neuropathic pain in a cohort of 17 burn survivors, an average of 16 months after burn. In contrast to our CRPS cohort, participants were more likely to be male (71%) and reported a higher level of psychological comorbidities (3/17 had dual diagnoses of depression and PTSD). Of those 6 patients completing the QDSA at baseline and after completing 3 months of treatment, a significant reduction in QDSA scores was reported (22.7% improvement, $P = .04$); however, no effect size was reported for comparison.²³ Our results in a predominantly female cohort suggest that gender is a statistically significant predictor of response to treatment, but the reasons for this are unknown, and 90% of the overall variance in the change in QDSA scores remains unaccounted for. Larger studies are required to build more powerful and stable models to predict treatment response and to inform the selection of persons likely to benefit from somatosensory rehabilitation.

A unique contribution of this study is the precise identification of the injured or damaged cutaneous nerve branches related to the territory of allodynia. Thirty-eight of 88 or 43% of the identified painful lesions were in the hand. Branches included the palmar cutaneous branches of both median and ulnar nerves, the dorsal cutaneous branch of the ulnar nerve and the superficial sensory branch of the radial nerve. However, despite the abundance of sensory end organs in the hand, this group of patients reported lower pain scores on the QDSA than did patients with nerve lesions in the forearm/arm or thoracic regions.

Another interesting finding of this study was the lack of association between overall self-reported pain (QDSA score) at baseline and the psychophysical measurement of severity of allodynia. This reflects previous research reporting weak correlations between quantitative testing of static and dynamic mechanical allodynia and overall pain scores in persons with CRPS.⁴⁵ In their sample of 145 persons with CRPS, Birklein et al⁴⁶ reported average MPQ scores (German version) of 20.4 (range: 0–63) and identified the presence of dynamic mechanical allodynia in 26% of this group but did not rate the severity of allodynia or compare pain scores for those with and without this symptom. The statistically significant but weak ($R^2 = 0.17$) relationship between the severity of allodynia (rainbow pain scale scores) and total area of the allodynic territory demonstrated here was not unexpected; this could be interpreted as support for the validity of the measures, as they are intended to measure different constructs.¹⁵ The mean increase in size of the allodynic territory predicted by an increase in the severity of allodynia as measured by the rainbow pain scale was also statistically significant but not clinically meaningful at 1.25 cm². Although the rainbow pain scale for severity of allodynia was not shown to be related to baseline pain, there was a statistically significant relationship ($P = .003$) between the rainbow pain score and the duration of distant vibrotactile counterstimulation required to see it resolve. This predicted duration of 24.4 days of treatment for every increase in allodynia severity can be used by therapists for treatment planning and to provide the client with evidence-informed expectations for outcome.

Limitations and areas for future research

Although the main outcome of this study draws on the QDSA, a well-validated self-report measure,²⁵ other analyses drew on measures such as allodyngraphy and the rainbow scale²¹ whose measurement properties are currently unknown (although this work is underway). Mapping techniques for documenting areas of altered sensation have a long history;^{19,47} several other techniques for mapping allodynia have also been recently described for CRPS and postherpetic neuralgia^{39,48} but without addressing the measurement properties of the technique.

The nature of a retrospective cohort drawn from clinical records has inherent bias. We sought to minimize aspects of this bias by including all available records for our baseline analyses and records with any follow-up for calculating change scores, regardless of whether the person had completed treatment. Furthermore, all data extraction and statistical analyses were conducted independently by TP, with oversight from the McMaster team but without involvement of the treating therapists at the Somatosensory Rehabilitation Centre. Because there was no control group, we were only able to retrospectively compare pre-post measures for the subjects in our cohort, which is considered as a weak form of support for effectiveness.⁴⁹ Other elements of potential inherent sampling bias are the fee-for-service nature of the treatment facility and the singular focus of the program on somatosensory rehabilitation, exclusive of other forms of rehabilitation. However, it is important to note that the model of alternating therapists for weekly treatment sessions reduces observer bias⁵⁰ and the training in assessment and treatment principles involved in the certification process for somatosensory therapists adds consistency.

This study provides estimates for effect size that will inform future prospective and controlled studies of the SRM for the treatment of allodynia. To achieve the sample sizes necessary to power these more rigorous evaluations, multisite studies will be required to recruit homogenous populations such as the group with CRPS of a single upper extremity described here. Future studies should include a broader spectrum of validated outcome measures addressing the key domains of pain and pain disability⁵¹ and facilitating comparison to other treatment methods that do not employ the SRM-embedded measurement techniques of allodyngography and the rainbow pain scale. Other potential populations with high incidence of allodynia include persons with postherpetic neuralgia⁴⁸ and women after breast cancer surgery^{52,53}; the potential of somatosensory rehabilitation to reduce pain and disability in these groups should also be explored.

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- #2. Data were collected from
- patient interviews
 - therapist examinations of patients
 - chart reviews
 - videography of patients during hand therapy sessions
- #3. The diagnosis of CRPS was established using the _____ criteria

- Budapest
 - Berlin
 - Bell
 - Brand
- #4. The area of allodynia was determined using _____ testing
- pin prick
 - monofilament
 - tuning fork
 - electrical
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