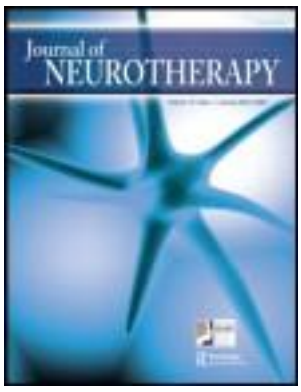

Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience

Neurofeedback Treatment for Pain Associated with Complex Regional Pain Syndrome Type I

Mark P. Jensen PhD [a] , Caroline Grierson RN [b] , Veronika Tracy-Smith PhD [c] , Stacy C. Bacigalupi MA [d] & Siegfried Othmer PhD [e]

[a] Department of Rehabilitation Medicine , University of Washington , Box 356490, Seattle, WA, 98195-6490, USA

[b] Train Your Brain , 941 Westwood Boulevard, Suite 206, Los Angeles, CA, 90024-2941, USA

[c] California State University , Fullerton, CA, USA

[d] Mount San Antonio College , 1100 North Grand Avenue, Walnut, CA, 91789, USA

[e] EEG Institute , 22020 Clarendon Street, Suite 305, Woodland Hills, CA, 91367, USA

Published online: 08 Sep 2008.

To cite this article: Mark P. Jensen PhD , Caroline Grierson RN , Veronika Tracy-Smith PhD , Stacy C. Bacigalupi MA & Siegfried Othmer PhD (2007) Neurofeedback Treatment for Pain Associated with Complex Regional Pain Syndrome Type I, Journal of Neurotherapy: Investigations in Neuromodulation, Neurofeedback and Applied Neuroscience, 11:1, 45-53, DOI: 10.1300/J184v11n01_04

To link to this article: http://dx.doi.org/10.1300/J184v11n01_04

Neurofeedback Treatment for Pain Associated with Complex Regional Pain Syndrome Type I

Mark P. Jensen, PhD
Caroline Grierson, RN
Veronika Tracy-Smith, PhD
Stacy C. Bacigalupi, MA
Siegfried Othmer, PhD

ABSTRACT. *Introduction*. Complex Regional Pain Syndrome Type I (CRPS-I) is a devastating pain condition that is refractory to standard care. Preliminary evidence suggests the possibility that neurofeedback training might benefit patients with chronic pain, including patients with CRPS-I. The current study sought to address the need for more information about the effects of neurofeedback on pain in persons with chronic pain by (1) determining the average decrease in pain in patients with CRPS-I following neurofeedback training, (2) identifying the percent of patients reporting pain decreases that are clinically meaningful, and (3) documenting other benefits of neurofeedback training.

Method. Eighteen individuals with CRPS-I participating in a multidisciplinary treatment program were administered 0-10 numerical rating scale measures of pain intensity at their primary pain site, as well as pain at other sites and other symptoms, before and after a 30 minute neurofeedback training session. A series of t-tests were performed to determine the significance of any changes in symptoms observed. We also computed the effect sizes and percent change associated with the observed changes in order to help interpret the magnitude of observed improvements in symptoms.

Results. There was a substantial and statistically significant pre- to post-session decrease in pain intensity at the primary pain site on average, with half of the study participants reporting changes in pain intensity that were clinically meaningful. Five of seven secondary outcome measures also showed statistically significant improvements following neurofeedback treatment.

Conclusions. The findings suggest that many patients who receive neurofeedback training report significant and substantial short-term reductions in their experience of pain, as well as im-

Mark P. Jensen is affiliated with the Department of Rehabilitation Medicine, Box 356490, University of Washington, Seattle, WA 98195-6490 USA.

Caroline Grierson is affiliated with the Train Your Brain, 941 Westwood Boulevard, Suite 206, Los Angeles, CA 90024-2941 USA.

Veronika Tracy-Smith is affiliated with the California State University, Fullerton, CA, USA.

Stacy C. Bacigalupi is affiliated with Mount San Antonio College, 1100 North Grand Avenue, Walnut, CA 91789 USA.

Siegfried Othmer is affiliated with EEG Institute, 22020 Clarendon Street, Suite 305, Woodland Hills, CA 91367 USA.

This research was supported in part by the Hughes M. and Katherine G. Blake Endowed Professorship in Health Psychology awarded to MPJ.

Address correspondence to: Mark P. Jensen, PhD, Department of Rehabilitation Medicine, Box 356490, University of Washington, Seattle, WA 98195-6490 USA (E-mail: mjensen@u.washington.edu).

The authors wish to thank Joshua Prager, MD, for his referral of patients for, and encouragement of, this project.

A brief presentation of some of the data from the participants in this study were reported in Othmer and Othmer (2006).

Journal of Neurotherapy, Vol. 11(1) 2007

doi:10.1300/J184v11n01_04

provements in a number of other pain- and nonpain-specific symptoms. The findings support the need for additional research to further examine the long-term effects and mechanisms of neurofeedback training for patients with chronic pain. doi:10.1300/J184v11n01_04

KEYWORDS. Complex Regional Pain Syndrome Type I, Reflex Sympathetic Dystrophy, neurofeedback

INTRODUCTION

Despite the fact that significant gains have been made in the understanding of chronic pain in the past few decades, there remain many individuals who continue to suffer from daily severe pain (Crombie et al., 1999; Ehde et al., 2003). None of the currently available treatments eliminates pain for the majority of patients who suffer from chronic pain (Turk, 2002). Even the most powerful analgesics provide no more than a 30% decrease in pain, on average, and the state-of-the art treatments rarely decrease severe pain to levels that are considered 'mild' (that is, 4 or less on a 0-10 scale) (Turk, 2002).

Complex Regional Pain Syndrome, Type I (CRPS-I, previously known as Reflex Sympathetic Dystrophy, or RSD), is a post-traumatic pain condition associated with local neurogenic inflammation (out of proportion to the injury) and severe pain in the skin, subcutaneous tissues and joints (Burton, Bruehl, and Harden, 2005). CRPS-I is particularly refractory to treatment. Very few treatments have been shown to be effective for CRPS-I (Perez, Kwakkel, Zuurmond, & de Lange, 2001), and no single treatment has been shown to be effective in a majority of patients (Quisel, Gill, & Witherell, 2005).

Evidence from a number of sources suggests that neurofeedback training may be helpful to some patients with chronic pain (Othmer & Othmer, 2006). For example, Caro and Winter (2001) report that 15 patients with fibromyalgia who received 40 or more sessions of neurofeedback (average = 58 sessions; range 40-98) all reported significant improvement in measures of attention, physician-assessed tenderness, self-reported pain, and fatigue. Recently, Sime (2004) presented a case report of a patient with trigeminal neuralgia treated with both neurofeedback (29 sessions) and peripheral biofeedback (10 sessions). She found that training at C3 was associated with improvements in sleep, and low reward frequency training at T3-T4 was associated with improvements in pain. In this case, the benefits of treatment allowed the patient to avoid a planned major surgery to treat the pain problem (severing the trigeminal nerve) and to discontinue the use of an opioid/acetaminophen combination analgesic. Moreover, the benefits of treatment were maintained in this patient at the 13-month follow-up.

Evidence from other studies similarly supports the idea that helping patients alter neurophysiological activity may result in pain reduction. For example, deCharms et al. (2005) reported that patients with chronic pain who learned to control relative activation in the rostral anterior cingulate cortex (an area associated with the processing and experience of pain) with the guidance of real-time fMRI feedback, reported decreases in their pain after training. Another group of investigators has shown in a group of 30 patients with fibromyalgia that providing electroencephalograph (EEG)-driven stimulation at a frequency that resulted in improvements in perceived mental clarity, mood, and sleep, also resulted in decreases in pain (Mueller, Donaldson, Nelson, & Layman, 2001).

Although the preliminary findings are promising, there are few published data concerning the effects of interventions that alter brain activity, such as neurofeedback, in patients with chronic pain. It is not known, for example, how many individuals with chronic pain respond to neurofeedback training with significant and

clinically meaningful decreases in pain. There is also a lack of clearly established neurofeedback treatment protocols that might be used for pain management. "Neurofeedback" can encompass a large variety of training protocols that can potentially include training patients to increase or decrease the density of many different frequency bandwidths from many different sites on the scalp.

Finally, although the primary goal when using neurofeedback training for patients with chronic pain is pain reduction, our patients report a number of other benefits of the neurofeedback training, such as decreased depression and anxiety, and improvement in overall well-being. Moreover, those of us who have treated patients with CRPS-I with neurofeedback, specifically (CG and VTS) have observed improvements in a number of non-pain symptoms associated with CRPS-I, such as muscle spasms, swelling, redness, and perceived tension at different pain sites. We were unable to identify any previous research that has documented the frequency and extent of improvements in these other symptoms in persons with CRPS-I.

The purpose of this study was to obtain additional information about the effects of neurofeedback on the pain reports of individuals with a chronic pain condition (in this case, CRPS-I). Specifically, we were interested in (1) determining the average decrease in pain reported by a consecutive series of patients with CRPS-I seen for neurofeedback training, (2) identifying the percent of these patients reporting pain decreases that are clinically meaningful, and (3) identifying and documenting other benefits of neurofeedback training that have been observed in clinical practice. Because many of the patients seen in this study were also participating in a comprehensive multidisciplinary 20-day CRPS-I treatment program that included other treatment modalities, we limited our data collection to before and after a single 30 minute neurofeedback session; a time period during which only neurofeedback was provided. In this way, any observed changes in symptoms could not be attributed to other pain interventions or treatments that some of the patients were receiving.

METHOD

Participants

The study participants were 18 patients with severe long-standing CRPS-I who were participating, or had participated in, a comprehensive 20-day CRPS-I treatment program. Patients participated in treatment four to six hours each day of the 20-day program, and each patient had an individualized schedule, depending on his or her treatment goals and needs. The treatment program included a number of components in addition to neurofeedback training, such as medication management, physical therapy and eclectic psychotherapy focused on pain issues. Because the participants were in various stages of their NF training when they were enrolled in the study, the specific session examined in this study varied widely (from the 7th to the 143rd; median = 20th). Many of the subjects were still in comprehensive pain treatment when they were recruited for this study, although some continued their neurofeedback training after the 20-day program ended. The patients who were in NF after comprehensive treatment were in a "maintenance" NF treatment phase designed to minimize pain flare-ups.

Most (90%, all but two) of the participants were female. Thirteen (72%) of the participants reported their race/ethnicity as Caucasian, three (17%) described themselves as Hispanic, one (6%) as Japanese-American, and another (6%) as African American. Their average age was 40.83 years (range, 17-56). The average duration of having a CRPS-I diagnosis was 2.89 years (range, 1-11 years). Six (33%) reported that they had CRPS-I symptoms in only one limb (three participants in one arm and three in one leg), seven (39%) in two limbs (one participant in both arms and six in one arm and one leg), one (6%) in three limbs (one arm and two legs), and four participants (22%) reported symptoms in all four limbs.

Neurofeedback Intervention Protocol

Neurofeedback training was performed using the NeuroCybernetics system (manufactured by EEG Spectrum International in Canoga Park, CA). This system affords a signal bandwidth of 0.5-30Hz; 12-bit digitization;

and digital filtering with infinite impulse response elliptic filters of second order. A nominal 3-Hz bandwidth is employed for the reward band for responsiveness. The center frequency is arbitrarily selectable. Inhibit bands are standard throughout: a combination of 2-13 Hz and of 14-30 Hz to cover the whole band. Feedback is provided to the client through visual, auditory, and tactile modalities.

Consistent with standard practice (e.g., Sime, 2004), the neurofeedback training protocol varied to some degree from patient to patient, and from session to session, to address the pain, other symptoms and issues raised by the patient (e.g., sleep problems, mood disturbance), and their reported reaction to the previous session's protocol. The neurofeedback sessions were all 30 minutes long. The number of training sites used in these sessions varied from 1 to 4, and included some combination of one or more of the following seven sites: P3-P4 (15 or 83% of the participants received this during some portion of their session), FP1-FP2 (9 or 50% participants received training at this site), T3-T4 (7 or 39%), FPO2-A2 (7 or 39%), CZ-FZ, (6 or 33%), F7-F8 (1 or 6%), and F3-F4 (1 or 6%). One participant (6%) received Alpha/Theta (A/T) training.

Current neurofeedback practice bases the selection of training sites and frequencies on cumulative clinical practice and experience. Adjustments in reinforcement frequencies are made on a patient-by-patient basis until the patient notes a positive response. We often begin treatment with bipolar placement at T3-T4 (ear ground) to stabilize brain activity, and as a way for many patients to obtain initial pain relief (cf. Sime, 2004; Othmer, 2005; Othmer & Othmer, 2006). In addition to pain relief, T3-T4 training is thought to encourage general arousal normalization, stabilization of mood, and general calmness (Putman, Othmer, Othmer, & Pollock, 2005). When training at T3-T4, we usually begin reinforcement at 12-15 Hz, and then move the reward frequency up or down by one full Hertz increment every three minutes (perhaps over the course of multiple sessions) with a goal of finding that state of arousal where the trainee feels optimally calm, alert, and euthymic. As the trainee progressively learns to discriminate these state shifts, finer adjustments are then made to render the patient most comfortable in the training. For some patients, the final reinforcement frequency might end up at very low levels. The reinforcement frequencies used in the seven patients who received bipolar T3-T4 training during the sessions examined in this study varied from 0.5-3.5 to 8.5-11.5.

Bipolar P3-P4 training is used to increase body awareness and for general physical calming and relaxation (Othmer, 2006). In addition, we have found that patients with chronic pain often report decreases in perceived pain with P3-P4 training. In the 15 participants who received P3-P4 training, the training frequencies ranged from 0-3 to 4-7 Hz, although we reinforced 0-3 Hz in a little over half of these (8 participants). We use bipolar training at FP1-FP2 to decrease obsessive thoughts and improve executive function, in general, and for patients with pain to decrease the focus on and general obsessiveness about the pain. In the current study, the training frequencies used for the FP1-FP2 training varied from 1-4 to 12-15 Hz, with the median being 4-7.

Bipolar CZ-FZ training usually provides a sense of deep calming, and decreases agitation, anxiety, and fear (Grierson, clinical observation), thus addressing the affective component of pain, although in our experience many patients with pain also report decreases in pain intensity with this training. The range of frequencies used for training in the six participants who received CZ-FZ training varied from 0-3 to 14-17 Hz, although all but one were 3.5-7.5 or less. Bipolar FPO2-A2 training is a means of training the right orbital frontal cortex, and can be helpful with patients who are experiencing fear (Othmer, 2006). FPO2 is a non-standard site in which the electrode is placed beneath the right eyebrow just at the bridge of the nose. Patients usually report feeling more "centered" and confident with this training. The range of frequencies used for the participants who received FPO2-A2 training in this study varied from 2.5-5.5 to 5.5-8.5 Hz (median, 4-7 Hz).

Bipolar F3-F4 training can be helpful for depressive symptoms and for patients with a low pain threshold (Othmer, 2006). Training at F3-F4 can also increase perceived energy. In the current study, the one patient who had this training was trained at 5.5-8.5 Hz. F7-F8 training may be helpful for patients with word finding difficulties or patients who feel "lost in the

drug fog." This training can be helpful for speech initiation and word fluency. One patient received F7-F8 training for a portion of the session examined in this study. Finally, alpha-theta training is useful for helping patients deal with trauma. One patient received alpha-theta training in the current study.

Measures

Primary outcome: Pain intensity. Just before and after one treatment session, the participants were asked to rate their pain intensity at up to four different sites (always starting with their primary pain problem) on 0 to 10 Numerical Rating Scales, with 0 = "No pain" and 10 = "Severe unbearable pain." Such scales have been shown to be valid as measures of pain intensity through their responsivity to effective pain treatments, as well as their consistent strong associations with other measures of pain intensity (Jensen & Karoly, 2001). All participants presented with one primary pain site, although many reported CRPS-I pain at multiple sites, and some participants also complained of non-CRPS-I pain.

Secondary outcome: CRPS-I symptoms and emotional functioning. In order to capture all of the potential CRPS-I symptoms and emotional functioning domains that might be affected by the training, the participants were asked to indicate whether or not they were experiencing any one of a number of CRPS-I symptoms (including swelling at the pain site, redness at the pain site, blueness at the pain site, pulling sensation at the pain site, muscle spasms, muscle tension, tics/jerking, cold skin, burning skin, deep aching and/or bone cold, skin sensitivity), their level of emotional distress (including depression, or anxiety), their level of emotional well-being (including feeling of well being, more centered), and any other symptoms or experiences that we have observed can be improved with neurofeedback treatment (headache, light sensitivity, sound sensitivity, mental clarity, energy level, relaxation). They were then asked to rate the magnitude of these symptom or experience domains on 0 - 10 NRSs before and after the session. The ratings that were used to assess secondary symptoms were developed specifically for this study, although similar measures have a long track record of demonstrating validity for symptom assessment (c.f. Jensen & Karoly, 2001; Cleeland et al., 2000). Not all participants reported pre- and post-session data for each symptom or outcome domain. Therefore, pre- to post-treatment ratings on the secondary outcome measures are only available for subsets of the 18 study participants.

Data Analysis

A paired t-test was performed to address the first study question concerning the extent of pre- to post-session decrease in pain. To help interpret the magnitude of any change observed, we also computed effect sizes for the pre- to post-session changes. Specifically, we computed effect sizes in standard deviation units (**d** = [pre- to post-session difference in rating]/ the pre-session standard deviation of the rating), interpreting a **d** of .2 as a "small" effect, a **d** of .5 as a "medium" effect, and a **d** of .8 (that is, a **d** that is close to a full standard deviation) as a "large" effect (Cohen, 1988).

To address the second study question, that is to identify the percent of participants who report pre- to post-session pain decreases that are clinically meaningful, we first computed the pre- to post-session percent change in pain for each participant. Given research that shows that changes in pain of at least 30% are deemed clinically meaningful by most patients (Farrar et al., 2001), we then determined the number and percent of participants whose percent improvement met or exceeded this criterion.

Finally, to address the third study question, that is, to identify other benefits of neurofeedback training, we repeated all of the analyses performed for the primary outcome variable for those symptoms for which we had pre- and post-session data from at least 10 participants. These included pain at secondary and tertiary sites, as well as perceived muscle spasms, muscle tension, feelings of deep ache, and overall well-being. A lower limit of data from 10 participants was selected because we deemed that as the minimum number necessary to provide an adequately reliable estimate of the changes that can occur in these symptoms with treatment. The alpha level selected for testing the statistical significance of changes in these sec-

ondary analyses were not corrected for multiple comparisons (i.e., the experimentwise alpha level was set at .05), given that such corrections would have severely decreased our ability to detect significant changes in the symptoms due to low sample size. However, to help interpret the findings, and as indicated above, we also computed effect sizes for these changes, and computed the percent of participants whose change in these symptoms was at least 30%.

RESULTS

Primary Outcome Variable: Pain Intensity

The results of the analyses testing the pre- to post-session change in pain intensity are presented in Table 1. As can be seen, there was a substantial (effect size, **d** = 1.03) pre- to post-session decrease in pain intensity at the primary pain site, with the rating decreasing, on average, 2.30 on the 0 - 10 scale. Moreover, the pain intensity ratings moved from what is considered a "moderate" level of pain (that is, 5.49, or between 5 and 6 on the 0-10 scale) to a "mild" level (3.19, between 1-4 on that same scale; Hanley et al., 2006; Serlin et al., 1995). Finally, half (9 of 18, or 50% participants) reported changes in pain intensity that were clinically meaningful; that is, that represented a 30% or more decrease from the pre-session pain levels.

Secondary Outcome Variables

Pre- and post-session ratings were available for 10 or more participants for seven of the secondary outcome measures: pain intensity at two additional sites, muscle spasm, muscle tension, a perceived deep ache, sensitive skin, and overall well-being. Statistically significant ($p < .05$) effects were found for 5 of these 7 secondary outcome variables. Two of the significant effects (for perceived muscle tension and well-being) were large ($\mathbf{d} \geq .8$; Cohen, 1988), two were moderate ($\mathbf{d} \approx .5$; for pain intensity at the second site and sensitive skin), and three were weak to moderate (**d** between .2 and .5; for pain intensity at the third site, muscle spasm, and deep ache). The rates of patients who reported clinically meaningful improvement in the secondary outcome variables generally reflect the effect sizes. Higher rates of clinically meaningful changes were found for improvement in muscle tension, well-being, and pain at the second site (54%, 40%, and 33%, respectively) than for pain intensity at the third site, muscle spasm, deep ache, and sensitive skin (10%, 27%, 27%, 10%, respectively). Still, for all but two of the outcome variables (pain intensity at the third site and sensitive skin), at least 25% of patients who provided data concerning the secondary variables reported clinically meaningful improvement in the secondary outcome domains.

DISCUSSION

A neurofeedback protocol that was tailored to address pain as well as each patient's symptoms was associated with substantial and clinically meaningful decreases in reported pain at the primary pain site for 50% of individuals who received this training. Moreover, after neurofeedback training, pain was in the mild range (less than 4 on a 0 - 10 scale) for the patients on average. This is difficult to achieve, even with the most powerful analgesics (Turk, 2002). The findings are consistent with the hypotheses that (1) mechanisms of central regulation of pain play a role in the pain experience of CRPS-I and (2) these mechanisms can be influenced by neurofeedback training, which is a self-regulation-based strategy.

The findings also demonstrated that the neurofeedback training was associated with improvements in pain in secondary pain sites, decreases in muscle spasm and tension, and improvements in overall well-being. The effect sizes were particularly large for improvements in perceived muscle tension and well-being. At the least, these findings indicate that patients with chronic pain who obtain neurofeedback training may obtain a number of beneficial "side effects" from this treatment that could contribute to an overall improvement in quality of life.

The findings are consistent with published case studies that suggest that biofeedback approaches, including neurofeedback, can be of help to patients with chronic pain (Barowsky, Zweig, & Moskowitz, 1987; Blanchard, 1979;

TABLE 1. Pre- and post-session means, change scores, sample sizes, effect sizes, significance levels of change, and percents of clinically meaningful change (30% or more) for the primary and secondary outcome measures.

Outcome domain	Pre-session Mean (SD)	Post-session Mean (SD)	Change score Mean (SD)	N of respondents	Effect size (**d**)	t (df)	Percent with meaningful improvement
			Primary outcome				
Primary pain site intensity	5.49 (2.24)	3.19 (2.72)	2.29 (2.35)	18	1.03	4.23 (17)†	50%
			Secondary outcomes				
Pain intensity: Site 2	4.93 (2.03)	3.87 (2.38)	1.07 (1.33)	15	.53	3.10 (14)**	33%
Pain Intensity: Site 3	5.50 (2.56)	4.55 (2.65)	0.95 (1.26)	10	.35	2.39 (9)*	10%
Muscle spasm	5.91 (2.84)	4.64 (2.84)	1.27 (1.42)	11	.45	2.97 (10)*	27%
Muscle tension	5.62 (1.66)	3.92 (2.33)	1.69 (1.18)	13	1.02	5.16 (12) ††	54%
Deep ache	6.68 (2.57)	5.68 (2.88)	1.00 (1.05)	11	.39	1.38 (10)	27%
Sensitive skin	6.35 (2.14)	5.30 (2.29)	1.05 (1.98)	10	.49	1.68 (9)	10%
Well-being	5.20 (2.45)	7.20 (2.37)	-2.00 (2.95)	15	.82	2.63 (14)*	40%

Note: **d** is expressed in standard deviation units, that is, d = pre-session minus post-session rating divided by pre-session standard deviation. Meaningful improvement is defined as a 30% more improvement (decrease in most symptoms, but increase in well-being) in the outcome measures, relative to pre-session levels.

*p < .05, **p < .05, †p = .001, ††p < .001

Sime, 2004), and suggest that current protocols recommending that thermal biofeedback be included as a treatment option for persons with CRPS-I (cf. Bruehl & Chung, 2006) be expanded to included neurofeedback as well. Certainly, the findings indicate that additional studies examining the effects of neurofeedback, perhaps relative to other treatments such as thermal feedback, are warranted.

The findings indicating benefits in multiple domains are consistent with the idea that individuals with chronic pain can have more global dysregulation(s) than just those related to the pain experience, and point to the possible existence of an integrated regulatory system where dysregulation in one domain could produce dysregulation in another. Alternatively, dysregulations in multiple systems could potentially have a common source. In either event, the findings indicate that it would be reasonable to expect that interventions, such as neurofeedback training, that promote self-regulation could have a multiplicity of benefits for what are typically seen as independent regulatory regimes. Thus, it is possible that one key to chronic pain in CRPS-I may lie in the organization of neuronal information transport and processing, in particular its organization in the timing, frequency, and spatial domains. The modulation of the pain response may therefore depend upon the balancing of excitatory and inhibitory influences on ascending pain pathways, and these could rely in turn on the quality of regulation of the relevant neuronal pathways.

The EEG neurofeedback technique can be viewed as a fairly generic stimulus that provokes the cerebral networks to alter their relative timing relationships, thus promoting a renormalization of function and enhancement of regulatory control (Othmer & Othmer, 2006). Current neurofeedback practice is empirical, with treatment protocols developed on a patient-by-patient basis. However, increased standardization concerning starting points for specific sites and reward frequencies is developing in the field. Using such starting points, sites are selected, and reward frequencies ad-

justed, until the patient reports feeling most calm, alert, stable and euthymic, with a goal that continued training in this way will promote calmness, stability, alertness and euthymia over the long term. To the extent that this condition promotes good regulation in terms of arousal, stability and emotional state, it should also promote better regulation of the pain response.

This study has a number of limitations that should be considered when interpreting the findings. A primary weakness is that all patients received neurofeedback training and there were no control patients. Thus, the benefits observed, although substantial, may not have been due entirely to the training. Simple regression to the mean or sitting quietly for 30 minutes could have contributed to the improvements that were observed. However, it should be noted that this study did provide an opportunity for the treatment to fail; that is, for no benefits to be observed, and neurofeedback passed this critical test. At the least, the findings support the potential for neurofeedback to be of help to patients with CRPS-I, are consistent with previous findings of effects of neurofeedback in patients with chronic pain (e.g., Caro & Winter, 2001; Sime, 2004), and indicate that additional research on these effects is warranted.

A second limitation of the study is the fact that multiple statistical tests were performed without control for alpha inflation associated with multiple tests. This was necessary to have adequate power to detect pre- to post-session differences in the symptoms assessed, given the limited sample size available. Still, five of the seven analyses were statistically significant, and in each case, the change observed was in the same direction; that is, showing improvements in symptoms. If no change in the symptoms tested were to occur with neurofeedback treatment in the population, one would expect only 5% of the tests to be statistically significant by chance alone. The high frequency (71%) of significant effects suggests that the changes were real.

Finally, we measured outcomes from pre- to post-session only, rather than pre- to post-multidisciplinary treatment. This was necessary in order to distinguish the effects of neurofeedback from the effects of the other interventions provided to these patients in the treatment program. Nevertheless, the data do not speak to the issue of how long the benefits of neurofeedback are maintained. Our clinical experience is that the changes in symptoms that occur with neurofeedback have both a transient component and a more permanent residual benefit, and that there is variability in both of these from patient to patient. Over time, and with ongoing training, many patients are able to exhibit a greater ability to impact on symptoms transiently as well as a greater tendency to hold their gains between sessions. This clinical observation is consistent with the findings reported by Sime (2004) in her single case study of a patient with trigeminal neuralgia. Related to this issue, one of us (VTS), when conducting A/T training, is now making audiotapes of the sounds that occur with this training (ocean waves and babbling brook sounds), and giving patients a CD or cassette tape of these sounds to listen to when they practice at home. Patients report that this has made the practice more effective, perhaps due to a conditioning effect of linking the sounds of training with its benefits. Longitudinal research is needed to determine the number of patients who are able to maintain the treatment gains made with neurofeedback, as well as identify the factors (e.g., number, density, and length of training sessions, use of cues such as audiotapes of sounds associated with training) that predict and contribute to better long-term outcomes.

Despite the study's limitations, the findings suggest that many patients who receive neurofeedback training report significant and substantial reductions in their experience of pain, as well as improvements in a number of other pain- and nonpain-specific symptoms. The results are consistent with the idea that pain in persons with CRPS-I may be related to dysregulation in brain systems, and that such dysregulation that can be improved with training using a neurofeedback protocol that has been found to be generally helpful in calming hyper-excitable and over-aroused nervous systems, as well as in promoting cerebral stability in general. The findings support the need for additional research to further examine the short- and long-term effects, and mechanisms, of neurofeedback training for chronic pain.

REFERENCES

Barowsky, E. I., Zweig, J. B., & Moskowitz J. (1987). Thermal biofeedback in the treatment of symptoms associated with reflex sympathetic dystrophy. *Journal of Child Neurology, 2*, 229-232.

Blanchard, E B. (1979). The use of temperature biofeedback in the treatment of chronic pain due to causalgia. *Biofeedback and Self-Regulation, 4*, 183-188.

Bruehl, S., & Chung, O. Y. (2006). Psychological and behavioral aspects of complex regional pain syndrome management. *Clinical Journal of pain, 22*, 430-437.

Burton, A. W., Bruehl, S., & Harden, R. N. (2005). Current diagnosis and therapy of complex regional pain syndrome: Refining diagnostic criteria and therapeutic options. *Expert Review of Neurotherapeutics*, 5, 643-651.

Caro, X. J., & Winter, E. F. (2001). Attention measures improve in fibromyalgia patients receiving EEG biofeedback training: A pilot study. *Arthritis and Rheumatism*, *44 (Supplement)*, S71.

Cleeland, C. S., Mendoza, T. R., Wang, X. S., Chou, C., Harle, M. T., Morrissey, M., & Engstrom, M. C. (2000). Assessing symptom distress in cancer: The M.D. Anderson Symptom Inventory. *Cancer, 89*, 1634-1646.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences, 2nd edition*. Hillsdale, NJ: Lawrence Erlbaum.

Crombie, I. K., Croft, P. R., Linton, S. J., Le Resche, L., & Con Korff, M. (Eds.). (1999). *Epidemiology of pain*. Seattle, WA: International Association for the Study of Pain Press.

deCharms, R. C., Maeda, F., Glover, G. H., Ludlow, D., Pauly, J. M., Soneji, D., Gabrieli, J. D. E., & Mackey, S. C. (2005). Control over brain activity and pain learned by using real-time functional MRI. *Proceedings of the National Academy of Science, 102*, 18626-18631.

Ehde, D. M., Jensen, M. P., Engel, J. M., Turner, J. A., Hoffman, A. J., Cardenas, D. D. (2003). Chronic pain secondary to disability: A review. *Clinical Journal of Pain, 19*, 3-17.

Farrar, J. T., Young, J. P., LaMoreaux, L., Werth, J. L., Poole, R. M. (2001). Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain, 94,* 149-158.

Hanley, M. A., Masedo, A., Jensen, M. P., Cardenas, D. D., & Turner, J. A. (2006). Pain interference in persons with spinal cord injury: Classification of mild, moderate, and severe pain. *Journal of Pain, 7,* 129-133.

Jensen, M. P., & Karoly, P. (2001). Self-report scales and procedures for assessing pain in adults. In D. C. Turk & R. Melzack (Eds.), *Handbook of pain assessment, 2nd edition*. New York: Guilford Publications, pp. 15-34.

Mueller, H. H., Donaldson, C. C. S., Nelson, D. V., & Layman, M. (2001). Treatment of fibromyalgia incorporating EEG-driven stimulation: A clinical outcomes study. *Journal of Clinical Psychology, 57*, 933-952.

Othmer, S.F. (2005). Inter-hemispheric EEG Training. *Journal of Neurotherapy, 9(2),* pp. 87-96.

Othmer, S., & Othmer, S. F. (2006). Efficacy of neurofeedback for pain management. In M. V. Boswell & B. E. Cole (Eds.), *Weiner's pain management: A practical guide for clinicians*, 7th edition. Boca Raton, FL: CRC Press, pp. 719-739.

Othmer, S. F. (2006). Protocol guide for neurofeedback clinicians: Optimizing electrode placements and reward frequencies through assessment and training, a Monograph. The EEG Institute, 22020 Clarendon St., #305, Woodland Hills, CA 91367.

Perez, R. S., Kwakkel, G., Zuurmond, W. W, & de Lange, J. J. (2001). Treatment of reflex sympathetic dystrophy (CRPS type 1): A research synthesis of 21 randomized clinical trials. *Journal of Pain and Symptom Management*, *21*, 511-526.

Putman, J. A., Othmer, S. F., Othmer, S., Pollock, V. E. (2005). TOVA Results Following Inter-Hemispheric Bipolar EEG Training, *Journal of Neurotherapy, 9(1)*, pp. 37-52.

Quisel, A., Gill, J. M., & Witherell, P. (2005). Complex regional pain syndrome: Which treatments show promise? *Journal of Family Practice*, *54*, 599-603.

Serlin, R., Mendoza, T., Nakamura, Y., Edwards, K., Cleeland, C. (1995). When is cancer pain mild, moderate or severe? Grading pain severity by its interference with function. *Pain, 61*, 277-284.

Sime, A. (2004). Case study of trigeminal neuralgia using neurofeedback and peripheral biofeedback. *Journal of Neurotherapy*, *8*, 59-71.

Turk, D. C. (2002). Clinical effectiveness and cost-effectiveness of treatments for patients with chronic pain. *The Clinical Journal of Pain, 18,* 355-365.

RECEIVED: 09/14/06
REVISED: 11/29/06
ACCEPTED: 12/28/06

doi:10.1300/J184v11n01_04