PSYCHOLOGICAL INTERVENTIONS

Stephen Bruehl, PhD

INTRODUCTION

Clinicians who work with complex regional pain syndrome (CRPS) patients recognize that successful management of the syndrome presents a significant challenge. In the absence of any definitive medical treatment,[1, 2] the need for multidisciplinary management of CRPS has been emphasized.[3] It is now generally agreed that successful treatment must simultaneously address the medical, psychological, and social aspects of the syndrome.[4] As will be described below, there are several reasons why addressing psychological and behavioral factors may be crucial to successful treatment in patients with CRPS. A rationale for use of psychological interventions in the management of CRPS will first be described. The treatment outcome literature regarding efficacy of psychological interventions for CRPS will then be presented, followed by a brief overview of relevant meta-analytic literature regarding efficacy of such interventions for non-CRPS chronic pain conditions. Finally, an overview of clinical recommendations for psychological care of CRPS patients based on both research literature and clinical experience will be presented.

HYPOTHESIZED LINKS BETWEEN CRPS AND PSYCHOLOGICAL FACTORS

The rationale for employing psychological interventions in CRPS patients derives generally from their recognized utility in management of non-CRPS chronic pain conditions, and more specifically, from theoretical pathways through which psychological and behavioral factors *might* directly interact with pathophysiological mechanisms believed to underlie CRPS. This latter theoretical rationale suggests the possibility that psychological interventions may not only be palliative in CRPS (which is almost assured), but also could have a *potentially* beneficial impact on underlying pathophysiology of the disorder in the context of multidisciplinary treatment.[5]

One pathway through which psychological factors could influence onset or maintenance of CRPS relates to the role of adrenergic mechanisms in the pathophysiology of CRPS. Diminished sympathetic outflow following peripheral nerve injury is believed to lead to localized upregulation of peripheral catecholaminergic receptors in the affected extremity.[6-8] This upregulation may lead to local hypersensitivity to circulating catecholamines, which in turn leads to excessive vasoconstriction,[6, 8-10] accounting for the characteristic cool, blue extremity typically seen in chronic CRPS. Following nerve injury like that which often triggers CRPS, primary afferent fibers may also become sensitive to adrenergic excitation, leading to increased nociceptive firing in response to sympathetic discharge or circulating catecholamines.[6, 11, 12] This catecholamine-induced nociceptive firing in turn is likely to contribute to central sensitization (by maintaining elevated nociceptive input), which may underlie the allodynia and hyperalgesia associated with CRPS.[13, 14] Central sensitization produces increased pain, which itself may provoke catecholamine release that further stimulates the nociceptive input maintaining the central sensitization, thereby producing a dysfunctional vicious cycle. The impact of catecholamine release in the pathophysiological mechanisms described above may be important to recognize given that psychological factors such as life stress and dysphoric emotional states (eg, anxiety, anger, depression) can be associated with increased catecholaminergic activity.[15, 16] For example, levels of

plasma epinephrine were found to correlate significantly with depressive symptoms in a sample of 16 CRPS patients.[17] It is theoretically plausible then that psychological factors such as these could, through their impact on catecholamine release, interact with adrenergically mediated pathophysiological mechanisms to contribute to onset or maintenance of CRPS.

Examination of the historical CRPS literature indicates frequent comments from authors indicating that psychological dysfunction (usually emotional disorders) was assumed to contribute to CRPS in at least some patients. This assumption often colored physicians' conceptualization of CRPS patients, despite the absence until 10 years ago of a significant body of controlled studies examining this issue. Examination of this literature indicates that nearly all studies assessing the role of psychological factors in CRPS have been limited to case series descriptions or cross-sectional psychological comparisons between CRPS patients and non-CRPS chronic pain patients.

Ability to make conclusions about psychological factors *contributing to onset* of CRPS depends on a prospective research design, and unfortunately, such designs are extremely rare in the CRPS literature. One recent prospective study indicated that higher levels of anxiety symptoms prior to total knee arthroplasty were associated with greater likelihood of displaying CRPS-like symptoms at 1 month postsurgery.[18] These latter findings would be consistent with the psychophysiological model proposed above. However, it is notable that neither anxiety nor depression predicted occurrence of CRPS-like symptoms at 6 months, so the long-term impact of psychological factors on development of chronic CRPS remains unclear. Even if the psychophysiological model is accurate, this should not be taken to imply that the presence of psychological "risk factors" alone would be either necessary or sufficient to cause CRPS. For example, one recent prospective study indicated that among 88 consecutive patients assessed shortly after acute distal radius fracture, 14 had significantly elevated life stress but did not develop CRPS, and the one patient who did develop CRPS had no apparent psychological risk factors (ie, no major life stressors, average emotional distress levels).[19]

In the absence of other prospective studies, the question of whether psychological factors affect the development and maintenance of CRPS must be addressed solely on the basis of case reports and retrospective or cross-sectional research designs which do not allow causation to be inferred. Two uncontrolled retrospective case series reported a relationship between onset of CRPS and contemporaneous emotional loss or major life stressors.[20, 21] The uncontrolled nature of these reports prevents any conclusions from being drawn regarding psychological factors as a contributor to onset of CRPS. The only controlled study regarding the role of life stress in CRPS onset[22] found that 80% of patients in a CRPS sample recalled a stressful life event temporally concurrent with the initiating physical trauma, in contrast to only 20% of non-CRPS controls. Although this suggests that stressful life events occurring concurrently with a physical trauma may contribute to development of CRPS, this study's findings still must be viewed with caution due to it being retrospective in nature. Though intriguing, there remain no prospective tests of this life stress hypothesis.

If psychological dysfunction is somehow uniquely involved in onset or maintenance of CRPS, one might expect increased prevalence of psychiatric disorders or elevated levels of emotional distress in this population. Based on structured interviews, estimates for prevalence of Axis I psychiatric disorders (eg, anxiety and depressive disorders) in CRPS patients indicate a prevalence ranging from 24% to as high as 46%.[23-25] It should be noted that only Monti et al (1998) included a non-CRPS chronic pain control group, and these authors reported that Axis I prevalence was not significantly higher in CRPS compared to non-CRPS pain patients.[23] Neither of the studies above documented

psychiatric status *prior to* CRPS onset and therefore cannot address the issue of causality. At present, there is no evidence that CRPS patients suffer from diagnosable psychiatric disorders at a higher rate than do other chronic pain patients.[26]

Controlled studies have also addressed the issue of whether CRPS patients are more emotionally distressed than other types of chronic pain patients. Several cross-sectional studies have found that CRPS patients report being more emotionally distressed than non-CRPS pain patients, in terms of depression and/or anxiety levels. These findings for depressed mood may be relevant when one considers that, in a study using time series diary methodology, depression levels on a given day have been found to be a significant predictor of CRPS pain intensity on the following day.[27]

More recently, results of a prospective study indicated that patients displaying signs and symptoms of CRPS 6 months following total knee replacement reported significantly higher levels of anxiety than did patients not displaying CRPS, despite the fact that both groups were continuing to experience at least some degree of pain.[17] However, *baseline* anxiety and depression did not predict CRPS status at 6 months, suggesting that the observed elevations in psychological distress were a result of CRPS pain rather than a cause. In light of these findings, one possible explanation for elevated distress often reported in CRPS patients relative to non-CRPS chronic pain patients might be that the unusual and sometimes dramatic symptomatology of CRPS (eg, allodynia, hyperalgesia, vasomotor changes, significant edema, motor changes) is more distressing than experiencing more common forms of chronic pain, and, moreover, the validity of these symptoms are often questioned by healthcare providers (who are more often than not misinformed about this condition), adding to patient stress.

Despite results of some studies suggesting that CRPS patients are more distressed than comparable non-CRPS chronic pain patients, it should be noted that several other studies have reported no such differences. For example, work by Ciccone and colleagues (1997)[28] provided only partial support for this hypothesis, finding that CRPS patients reported more somatic symptoms of depression than non-CRPS patients with local neuropathy, but displayed no emotional differences relative to low back pain patients. Other studies have found no evidence of elevated distress among CRPS patients compared to low back pain patients[29, 30] or headache patients.[29] These negative results suggest the possibility that rather than CRPS being associated inherently with greater distress, the inconsistent findings regarding this issue may be accounted for by differences in sample selection, pain duration, clinic referral patterns, and specific psychometric measures used across studies. In the absence of additional well-controlled studies, it remains unclear whether the findings suggesting uniquely elevated distress in CRPS patients are an artifact of sample selection.

Whether or not absolute levels of dysphoric emotional states are elevated in CRPS patients has been evaluated in two studies, which found that emotional distress, when present, may have a greater impact on pain intensity in CRPS than in other types of chronic pain.[26, 31] For example, correlations between pain intensity and both anxiety and anger expressiveness have been found to be significantly stronger in CRPS patients than in non-CRPS chronic pain patients.[26, 31] These results suggest that even if CRPS patients are not uniquely distressed, the impact of that distress may be unique, possibly due to the hypothesized adrenergic interactions described above. These findings could have significant treatment implications, as psychological interventions that reduce distress may directly contribute to reductions in CRPS symptoms (eg, pain, vasomotor changes).

Another important pathophysiological mechanism that may contribute to CRPS is the sometimes dramatic disuse that patients develop in an effort to avoid stimuli that may trigger hyperalgesia and allodynia in the affected extremity. Even in healthy individuals, prolonged disuse alone may lead to temperature/color changes and hyperalgesia similar to those observed in CRPS.[32] Diminished active range of motion is common even in early CRPS,[33] and CRPS is associated with significantly reduced mobility and impaired ability to use the affected area normally.[34] Significant inverse correlations between CRPS pain intensity and ability to carry out activities of daily living[22] suggest that pain avoidance is likely one of the common reasons for CRPS-related activity impairments. Learned disuse, reinforced by either avoidance of actual pain or reduced anxiety subsequent to avoiding *anticipated* pain exacerbations, may prevent desensitization and eliminate the normal tactile and proprioceptive input from the extremity that may be necessary to restore normal central signal processing.[35] Learned disuse may also inhibit the natural movement-related pumping action that helps prevent accumulation of catecholamines, tachykinins, and other nociceptive and inflammatory mediators in the affected extremity, which may impact negatively on CRPS signs and symptoms (eg, [11] and [35]). Pain-related learned disuse might therefore interact with other pathophysiological mechanisms to help maintain and exacerbate both the pain-related and autonomic features of CRPS.[5]

In summary, while the contribution of psychophysiological interactions to CRPS is largely speculative, it is theoretically consistent and highlights the importance of addressing psychological factors in the clinical management of CRPS. A vicious cycle in which pain provokes disuse and emotional arousal, both of which in turn further exacerbate the pain, could contribute to maintenance of CRPS. Psychological/behavioral treatments therefore play an important role in CRPS management by targeting learned disuse and both life stress and emotional distress that may contribute to maintenance or exacerbation of the disorder. Moreover, such treatments can enhance pain coping skills that ultimately lead to improved functioning and quality of life and increase ability to self-manage pain. At minimum, such treatments are likely to enhance patients' sense of control over the condition, and thereby reduce fears that may be a barrier to achieving success in functional therapies.

EFFICACY OF PSYCHOLOGICAL INTERVENTIONS IN CRPS PATIENTS

A review of the Medline and CINAHL databases reveals a number of studies that have addressed efficacy of psychological interventions for CRPS, although nearly all of these reflect uncontrolled designs that permit only limited conclusions to be drawn. An additional caveat regarding these studies is that the criteria used to diagnose CRPS were often not adequately described and in all likelihood varied substantially across studies. This lack of consistent or specified diagnostic criteria limits the ability to generalize these results to patients diagnosed according to current IASP criteria.

A summary of studies reporting on efficacy of psychological treatments for CRPS is presented in Table 1. This table reveals that only one randomized trial specifically testing psychological interventions in CRPS patients has been published to date. Fialka et al (1996)[37] randomized treatment for 18 CRPS patients to receive either home physical therapy (PT) or home PT plus once-weekly autogenic relaxation training for 10 weeks. Both groups showed similar improvements in pain, range of motion, and edema, although patients in the PT+Autogenics group demonstrated significantly greater improvements in limb temperature.[37] Although low statistical power due to the small sample limited the ability to adequately evaluate intervention efficacy, these results suggest that relaxation-based interventions may have some benefit in management of CRPS.

Results of several published case studies and small case series further suggest that the pain of CRPS may be reduced through use of a variety of psychological techniques. For example, Barowsky et al (1987)[38] reported on a 12-year-old CRPS patient in whom ten sessions of thermal biofeedback resulted in resolution of CRPS that had been resistant to previous treatments. Alioto (1981)[39] reported that an adult chronic CRPS patient experienced a 75% decrease in pain intensity and improved mood subsequent to a series of psychological training sessions incorporating autogenic relaxation, breathing relaxation, and muscular and temperature biofeedback. Total elimination of pain was reported by this same author in a 16-year-old CRPS patient using a similar intervention approach.[39] Dramatic improvements like those cited above were also noted in an adult chronic CRPS patient described by Blanchard (1979).[40] Eighteen sessions of thermal biofeedback training resulted in nearly complete elimination of pain, as well as the ability to raise digital temperature in the affected hand by 1.5 degrees C.[40] This relief was reported to be maintained at 1-year follow-up. Autogenic relaxation and imagery training (6 sessions) has been reported to result in complete resolution of CRPS-related pain of 7 months duration in a 15-year-old patient, with these gains reportedly maintained at 18-month follow-up.[41] Hypnotic imagery combined with relaxation techniques (over a 6-9 month period) has additionally been reported to result in complete resolution of CRPS symptoms in a series of three adult CRPS patients.[42] It should be noted that the complete resolution of symptoms described in some cases above using only psychological interventions is likely to be atypical and fails to recognize the number of less dramatic successes—or even treatment failures—no doubt encountered by these same authors. While the uncontrolled designs used in the studies described above prevent definitive conclusions from being drawn regarding the efficacy of psychological techniques for CRPS, they clearly support the recommendation that such techniques may play an important role in effective interdisciplinary treatment.

Other research has addressed the multidisciplinary aspects of treatment, suggesting that integration of psychological methods with medical and physical therapy may be helpful in managing CRPS.[43-45] Two randomized controlled trials (RCTs) examining efficacy of physical therapy for CRPS have included components of psychological treatment in the therapy package.[43, 44, 46] For example, Oerlemans et al (1999; 2000)[43, 44] tested a physical therapy protocol that included relaxation exercises and cognitive interventions (designed to increase perceived control over pain). This combined intervention was found to produce significantly greater improvements in pain, active range of motion, and impairment levels than were observed in the social work control group.[43, 44] In another randomized controlled trial of physical therapy, Lee et al (2002)[46] examined two different frequencies of physical therapy treatment (once per week versus three times per week) for child and adolescent CRPS patients, with both groups additionally receiving six sessions of cognitive behavioral treatment. Although no attentional control group was available for comparison, both groups were found to improve significantly in terms of pain and function when compared to their pretreatment baselines. While the multicomponent interventions in both of these studies do not permit conclusions to be drawn specifically regarding the efficacy of psychological interventions, they do suggest that psychological treatment in combination with physical therapy may prove effective in a rehabilitation-focused approach to management of CRPS.

Uncontrolled trials also support inclusion of psychological interventions in the multidisciplinary treatment package, although all of these studies are in child or adolescent populations. For example, Wilder et al (1992)[47] described a conservative multidisciplinary treatment program used in 70 childhood CRPS patients that incorporated relaxation training and cognitive-behavioral interventions, noting that it resulted in improved pain and functioning

in 57% of the sample. Even more impressive results were reported by Sherry et al (1999)[45] in a case series of 103 primarily adolescent CRPS patients. Multidisciplinary treatment incorporating conservative medication management, regular active physical therapy, and psychological counseling (for 77% of the sample) reportedly resulted in 92% of this sample achieving symptom-free status.[45] Although no details are provided, Wesdock et al (1991)[48] noted that biofeedback was helpful in some cases of short-duration childhood CRPS in the context of multidisciplinary treatment.

Although not entirely relevant regarding the specific issue of psychological interventions for CRPS, two other studies do bear mention. The first is a small randomized controlled trial comparing efficacy of a motor imagery intervention (n=7) for CRPS patients to a "standard treatment" control group (n=6).[49] This intervention focused on requesting that patients make repeated imaginal movements of the CRPS affected limb (throughout the day) to match pictured movements. Despite the small sample, results indicated that the motor imagery intervention resulted in significantly greater improvements in pain intensity than did standard treatment. Although the imagery used (movement) was not identical in character to that most frequently used in psychological interventions (pain reduction or relaxing imagery), these findings do highlight the potential benefits of imagery interventions for CRPS management.

A second study is important given the nearly complete absence of RCTs of psychological interventions in any specific type of neuropathic pain, CRPS or otherwise. In a small, six-session randomized controlled trial in patients with HIV-related neuropathic pain, Evans et al (2003)[50] compared the efficacy of cognitive behavioral therapy (n=12) to supportive therapy (n=21). Results indicated that cognitive behavioral therapy resulted in greater reductions in distress and greater reductions in pain and pain-related interference than were observed in the supportive therapy group (although results for pain-related measures were not statistically significant due to the small sample size). At minimum, these results support the notion that psychological interventions generally used for treatment of a variety of nonneuropathic pain conditions are also likely to work for neuropathic pain conditions such as CRPS.

In summary, although to date there is only one small randomized controlled trial specifically testing the efficacy of psychological interventions for CRPS, the multitude of clinical case reports available do suggest that psychological interventions are likely to be a useful part of a comprehensive multidisciplinary treatment program. The efficacy of such techniques for CRPS would not be surprising, given the strong evidence of their utility in other types of chronic pain. These results will be briefly summarized below.

EFFICACY OF PSYCHOLOGICAL INTERVENTIONS IN NON-CRPS CHRONIC PAIN DISORDERS

Numerous RCTs have documented the efficacy of various psychological approaches to the management of chronic pain in general, and these have been quantitatively summarized in several published meta-analyses. Treatment approaches examined include many of the same interventions used in the CRPS studies described previously, including relaxation techniques, autogenic training, biofeedback, behavioral therapy, and cognitive behavioral therapy. Results of several meta-analyses clearly document the efficacy of these techniques for non-CRPS chronic pain conditions. For example, a meta-analysis of clinical trials testing progressive muscle relaxation techniques found significant effects in various chronic pain conditions, reflecting a moderate effect size.[51] Meta-analysis specifically of

autogenic training, another self-relaxation procedure, also indicated a significant and at least moderate effect size in controlled trials for patients with headache and somatoform pain disorder.[52] Significant efficacy for biofeedback training is also indicated by meta-analyses in populations including temporomandibular joint pain and migraine headache patients.[53, 54] More generally, meta-analyses of RCTs across psychological treatment types (various treatments provided both alone and in combination) indicate significant efficacy of this class of techniques for a variety of chronic pain conditions, including low back pain, fibromyalgia, rheumatoid arthritis, and cancer-related pain.[55-61] Results of one available meta-analysis also confirm that behavioral and cognitive behavioral interventions are significantly effective for children and adolescents with chronic pain.[62] Overall, the results of RCTs of psychological treatment approaches consistently indicate a benefit, in terms of experienced pain, mood, and function, for patients with a variety of chronic pain conditions. Given the proven efficacy of these interventions for various non-CRPS chronic pain conditions, their utility specifically in the management of CRPS might also be expected. These meta-analytic findings provide additional support, albeit indirect, for the reported efficacy of psychological interventions in CRPS patients described in uncontrolled trials.

CLINICAL RECOMMENDATIONS

There is little well-controlled CRPS-specific outcome research on which to base psychological treatment recommendations for the condition. However, clinical experience and available data do suggest several specific strategies that may be helpful. A suggested psychological intervention algorithm is summarized in Figure 1.

While there are indications that many cases of acute CRPS may resolve relatively quickly without any need for specific psychological intervention, one intervention recommended for all *acute or chronic* CRPS patients is comprehensive education about the condition. Specifically, this low-cost intervention is recommended for all patients *and their families,* such that they receive detailed information early in treatment that addresses what is known about CRPS, the negative effects of disuse, the importance of reactivation, and the need for an active self-management approach to treatment. This education should also provide an explanation of how possible psychophysiological interactions could affect severity of CRPS. Such education may help prevent development of dysfunctional behavior patterns (eg, elevated distress and severe disuse) that could contribute to the severity, disability, and chronicity of the condition. For more chronic CRPS patients or those who do not respond to limited intervention, individualized psychological evaluation is recommended, followed by focused psychological pain management treatment. An overview of several key issues to address in this assessment and treatment is provided below.

ASSESSMENT

Several specific areas of relevance to CRPS management should be addressed in the psychological evaluation, including: 1) presence of comorbid Axis I psychiatric disorders, 2) cognitive, behavioral, and emotional responses to CRPS, 3) ongoing life stressors, and 4) responses by significant others to the patient's CRPS. As noted previously, Axis I psychiatric disorders such as Major Depression, Panic Disorder, Generalized Anxiety Disorder, and Posttraumatic Stress Disorder are at least as common in CRPS patients as in other chronic pain patients.[23] The importance of assessing for disorders such as major depression is highlighted by the fact that diminished energy level

and motivation related to clinical depression may be a significant barrier to success in active, physically focused treatment modalities (eg, physical and occupational therapy). Identification of specific life stressors and general emotional arousal (depressed, anxious, fearful, or angry mood), even in the absence of clinically diagnosable psychiatric disorder, may be equally important given possible psychophysiological interactions hypothesized above.

Research in chronic back pain patients indicates that pain-related disability is more strongly related to *fear* of pain than it is to the level of pain intensity itself. Therefore, assessment of CRPS patients' fear of their pain is also important. Evidence from studies in chronic back pain patients indicates that pain-related fear contributes to elevated pain intensity and disability in part by leading to chronic guarding, bracing, and disuse in response to fears that movement will lead to increased pain and reinjury.[63] This is particularly important for CRPS patients, in whom disuse may interact directly with the pathophysiology of the disorder, and in whom severe guarding may contribute to secondary proximal myofascial pain that can mimic spreading of the disorder (and further increase fear). Not all activity avoidance in CRPS patients is unreasonable (eg, avoiding heavy lifting with the affected hand), and therefore the focus should be on identifying activity avoidance that is extreme and unreasonable. For example, some CRPS patients may appear to be experiencing agoraphobia based on their reports of an intense desire to avoid crowded environments. However, further assessment in many cases reveals that this avoidance is motivated by excessive fears that someone will accidentally make contact with the affected extremity and provoke extreme pain. While patients admit that this is unlikely to occur, the behavior persists. This pattern highlights the fact that activity avoidance and disuse in chronic pain can be operantly reinforced by the decreased fear that accompanies avoidance of expected pain exacerbations.[64]

Assessment of the cognitive impact of CRPS should include thorough exploration of the patient's beliefs regarding CRPS. Several misconceptions are common among patients, particularly those who have failed previous treatments and among those who search for answers on the internet. For example, patients may believe that CRPS is an untreatable, progressively deteriorating condition, and that it will necessarily spread throughout the body (a belief not supported by empirical studies). Catastrophic cognitions such as these are often a contributor to negative emotional states that may have a deleterious impact on CRPS and responses to treatment. The importance of addressing catastrophic cognitions in CRPS treatment is highlighted by results of a prospective study in non-CRPS neuropathic pain patients, which indicated that level of catastrophizing at study baseline predicted level of pain 8 weeks later, independent of baseline pain and depression.[65] Patients may also possess incorrect beliefs regarding the meaning of CRPS pain. Not surprisingly given the intensity and unusual nature of allodynic pain, patients may assume that pain signals damage, and as a corollary, "if it hurts, don't do it." Such beliefs may be a primary contributor to pain-related fear, and consequently, exacerbate disuse. It is therefore important that patients understand that neuropathic pain as in CRPS does not signal tissue damage. Unrealistic beliefs regarding how CRPS treatment should progress may also be problematic. Common misconceptions include beliefs that sympathetic blocks alone are curative, and that treatments that exacerbate pain temporarily cannot contribute to long-term improvements. Invasive and expensive interventional procedures, such as spinal cord stimulation and intrathecal pumps, may prove valuable for some patients in the later stages of treatment. However, excessive focus early in treatment upon invasive interventions viewed as a "quick fix" before patients have participated in a comprehensive multidisciplinary program leads to reduced motivation to engage actively in multidisciplinary care, and outcomes are likely to suffer.

PSYCHOLOGICAL PAIN MANAGEMENT INTERVENTION

The pain management intervention component of CRPS treatment should include relaxation training (preferably in conjunction with thermal and/or electromyographic biofeedback), training in cognitive pain coping skills, and behavioral intervention to address disuse and activity avoidance issues, as well as family reinforcement issues. In addition to the above, other targeted cognitive behavioral therapy interventions may be helpful if specific issues are identified during evaluation that may impact on the condition or ability to engage effectively in treatment (eg, major ongoing life stressors or Axis I psychiatric disorders).

The goal of relaxation training with biofeedback is to increase patients' ability to control their pain and decrease emotional arousal (and associated sympathetic discharge) that may impact negatively on the condition. Clinical trial data in non-CRPS chronic pain suggest that breathing-focused relaxation, progressive muscle relaxation, relaxing imagery, and autogenic training all may prove beneficial. There is no clear evidence of the superiority of any one of these interventions, and thus the specific techniques employed are generally determined by patient and therapist preference. With all relaxation/biofeedback techniques, the key factor determining their clinical efficacy is the degree to which patients practice the techniques at home and integrate them into their pain coping during regular activities on a daily basis.

A second aspect of the pain management treatment component is cognitive intervention. Given the emphasis in recent consensus guidelines for CRPS management using an active rehabilitation approach, it is important to reframe the CRPS patient's role as that of an active participant in the treatment process rather than a passive recipient of treatment interventions. As part of this active treatment focus, pain exacerbations should be identified as a cue to practice self-management interventions that may help patients gain control over their situation. As patients learn relaxation skills and begin to understand the cognitive and behavioral aspects of the syndrome, they will have increasing resources for exerting at least some degree of control over their CRPS. Increased sense of perceived control, even if that control is limited in scope, may be an important factor in determining outcomes in chronic pain treatment (eg, see [66]). Dysfunctional cognitions may be common in CRPS patients,[26] including catastrophic interpretations about symptoms or implications of CRPS for the future, fearful pain-related cognitions like those described above, and unrealistic beliefs about treatment. Such cognitions can contribute to elevated distress, which may have an impact on sympathetic outflow and catecholamine release, and thereby aggravate CRPS pain and vasomotor changes. Moreover, in the absence of *in vivo* reactivation experiments in which constructive self-talk is practiced, fear of pain may prevent improved daily function even in the face of objectively improved capabilities during therapy. It is therefore important that cognitive interventions be employed to help patients learn to identify and modify their specific dysfunctional cognitions regarding reactivation, CRPS, and its treatment.

Given the impact of learned disuse as a potential barrier to reactivation, behavioral interventions targeting this disuse can also be an integral component of the overall treatment program. Reactivation and behavioral goals must necessarily balance disuse concerns with avoiding severe pain exacerbations that could potentially contribute to maintenance of CRPS and reinforce learned disuse. *Realistic* pain-limited incremental reactivation is key, with the psychologist and functional therapists coordinating efforts to ensure that appropriate activity goals are set and that problems encountered in this reactivation process are effectively addressed.

With regards to family intervention, the most crucial issue to address is the possibility that some family members may be a barrier to reactivation due to solicitous responses and fear of pain exacerbations. Unless detailed education regarding CRPS and disuse issues is provided, family members may consider any activity that increases pain as dangerous to the patient and something to be discouraged. It is therefore important to ensure that family members understand the necessity of reactivation and that this might be associated with transient increases in pain. In contrast, family members may, due to a lack of understanding, incorrectly assume that unusual symptoms such as allodynia are exaggerated, and as a consequence, be less than fully supportive. Adequate positive family support can have a significant impact on ultimate efficacy of treatment. Family members should therefore be guided in how they can best respond to the patient's pain in a way that encourages and facilitates appropriate reactivation, and helps keep the patient focused on constructive management of the condition. The importance of addressing family issues is highlighted by findings demonstrating that more than half of caregivers of CRPS patients experience negative mood and significant strain, and these factors in turn are associated with greater patient disability.[67] While one might assume that this family distress and strain is a *result* of having to handle greater patient disability, the possibility of bi-directional causal influences must at least be considered.

SUMMARY

There is no solid evidence that psychological factors are necessarily involved in the onset of chronic CRPS. However, there are theoretically plausible pathways through which psychological factors in some cases *could* affect the development of CRPS. Evidence is mixed that CRPS patients are in any way psychologically unique compared to other chronic pain patients, although the hypothesis that they are as a group more emotionally distressed has received some support. Once CRPS has developed, emotional factors may have a greater impact on CRPS pain intensity than in non-CRPS pain conditions, possibly through the impact of dysphoric psychological states on catecholamines. Meta-analytic reviews document the efficacy of various psychological interventions for many types of non-CRPS chronic pain, and suggest that such interventions are likely to be beneficial for CRPS patients as well. Adequate randomized controlled studies of psychological interventions in CRPS patients are not available to guide this aspect of CRPS management, although numerous uncontrolled studies suggest the likely utility of several approaches. These approaches include various forms of relaxation training, biofeedback, and cognitive and behaviorally focused interventions. Successful implementation of these interventions requires recognition of the unique issues in CRPS patients, particularly the pervasive learned (or centrally mediated) disuse often seen in such patients. Clinical experience using techniques like those described above in an integrated multidisciplinary context indicates that many CRPS patients can achieve significant improvements in functioning and ability to control pain.

REFERENCES

1. Kingery WS. A critical review of controlled clinical trials for peripheral neuropathic pain and complex regional pain syndromes. *Pain.* 1997;73:123-139.
2. Perez RS, Kwakkel G, Zuurmond WW, de Lange JJ. Treatment of reflex sympathetic dystrophy (CRPS type 1): a research synthesis of 21 randomized clinical trials. *J Pain Symptom Manage.* 2001;21:511-526.
3. Grabow TS, Christo PJ, Raja SN. Complex regional pain syndrome: diagnostic controversies, psychological dysfunction, and emerging concepts. *Adv Psychosom Med.* 2004;25:89-101.
4. Stanton-Hicks M, Bruehl SP, Carr DB, et al. Updated interdisciplinary clinical pathway: report of an expert panel. *Pain Practice.* 2002;2:1-16.
5. Bruehl S. Do psychological factors play a role in the onset and maintenance of CRPS? In: Harden R, Baron R, Janig W, eds. *Complex Regional Pain Syndrome.* Seattle, Wash: IASP Press; 2001.
6. Harden RN, Duc TA, Williams TR, Coley D, Cate JC, Gracely RH. Norepinephrine and epinephrine levels in affected versus unaffected limbs in sympathetically maintained pain. *Clin J Pain.* 1994;10:324-330.
7. Birklein F, Riedl B, Claus D, Neundorfer B. Pattern of autonomic dysfunction in time course of complex regional pain syndrome. *Clin Auton Res.* 1998;8:79-85.
8. Kurvers H, Daemen M, Slaaf D, et al. Partial peripheral neuropathy and denervation induced adrenoceptor supersensitivity: functional studies in an experimental model. *Acta Orthopaedica Belgica.* 1998;64:64-70.
9. Arnold JM, Teasell RW, MacLeod AP, Brown JE, Carruthers SG. Increased venous alpha-adrenoceptor responsiveness in patients with reflex sympathetic dystrophy. *Ann Intern Med.* 1993;118:619-621.
10. Baron R, Maier C. Reflex sympathetic dystrophy: skin blood flow, sympathetic vasoconstrictor reflexes and pain before and after surgical sympathectomy. *Pain.* 1996;67:317-326.
11. Drummond PD, Finch PM, Skipworth S, Blockey P. Pain increases during sympathetic arousal in patients with complex regional pain syndrome. *Neurology.* 2001;57:1296-1303.
12. Jänig W, Baron R. The role of the sympathetic nervous system in neuropathic pain: clinical observations and animal models. In: Hansson P, Fields H, Hill R, Marchettini P, eds. *Neuropathic Pain: Pathophysiology and Treatment.* Seattle, Wash: IASP Press; 2001.
13. Gracely RH, Lynch SA, Bennett GJ. Painful neuropathy: altered central processing maintained dynamically by peripheral input. *Pain.* 1992;51:175-194.
14. Woolf CJ, Shortland P, Coggeshall RE. Peripheral nerve injury triggers central sprouting of myelinated afferents. *Nature.* 1992;355:75-78.
15. Charney DS, Woods SW, Nagy LM, Southwick SM, Krystal JH, Heninger GR. Noradrenergic function in panic disorder. *J Clin Psychiatry.* 1990;51 (Suppl A):5-11.
16. Light KC, Kothandapani RV, Allen MT. Enhanced cardiovascular and catecholamine responses in women with depressive symptoms. *Int J Psychophysiol.* 1998;28:157-166.
17. Harden RN, Rudin NJ, Bruehl S, et al. Increased systemic catecholamines in complex regional pain syndrome and relationship to psychological factors: a pilot study. *Anesth Analg.* 2004;99:1478-1485.
18. Harden RN, Bruehl S, Stanos S, et al. Prospective examination of pain-related and psychological predictors of CRPS-like phenomena following total knee arthroplasty: a preliminary study. *Pain.* 2003;106:393-400.
19. Dijkstra PU, Groothoff JW, ten Duis HJ, Geertzen JH. Incidence of complex regional pain syndrome type I after fractures of the distal radius. *Eur J Pain.* 2003;7:457-462.
20. Van Houdenhove B. Prevalence and psychodynamic interpretation of premorbid hyperactivity in patients with chronic pain. *Psychother Psychosom.* 1986;45:195-200.
21. Egle UT, Hoffmann SO. [Psychosomatic correlations of sympathetic reflex dystrophy (Sudeck's disease). Review of the literature and initial clinical results]. *Psychother Psychosom Med Psychol.* 1990;40:123-135.
22. Geertzen JH, de Bruijn-Kofman AT, de Bruijn HP, van de Wiel HB, Dijkstra PU. Stressful life events and psychological dysfunction in complex regional pain syndrome type I. *Clin J Pain.* 1998;14:143-147.
23. Monti DA, Herring CL, Schwartzman RJ, Marchese M. Personality assessment of patients with complex regional pain syndrome type I. *Clin J Pain.* 1998;14:295-302.
24. Rommel O, Malin JP, Zenz M, Janig W. Quantitative sensory testing, neurophysiological and psychological examination in patients with complex regional pain syndrome and hemisensory deficits. *Pain.* 2001;93:279-293.
25. Hardy M, Merritt W. Psychological evaluation and pain assessment in patients with reflex sympathetic dystrophy. *J Hand Ther.* 1988;1:155-164.
26. Bruehl S, Husfeldt B, Lubenow T, Nath H, Ivankovich AD. Psychological differences between reflex sympathetic dystrophy and non-RSD chronic pain patients. *Pain.* 1996;67:107-114.
27. Feldman SI, Downey G, Schaffer-Neitz R. Pain, negative mood, and perceived support in chronic pain patients: a daily diary study of people with reflex sympathetic dystrophy syndrome. *J Consult Clin Psychol.* 1999;67:776-785.
28. Ciccone DS, Bandilla EB, Wu W. Psychological dysfunction in patients with reflex sympathetic dystrophy. *Pain.* 1997: 71: 323-333.
29. DeGood DE, Cundiff GW, Adams LE, et al. A psychosocial and behavioral comparison of reflex sympathetic dystrophy, low back pain and headache patients. *Pain.* 1993;54:317-322.
30. Haddox JD, Abram SE, Hopwood MH. Comparison of psychometric data in RSD and radiculopathy. *Reg Anesth.* 1988;13:27.
31. Bruehl S, Chung OY, Burns JW. Differential effects of expressive anger regulation on chronic pain intensity in CRPS and non-CRPS limb pain patients. *Pain.* 2003;104:647-654.
32. Butler S. Disuse and complex regional pain syndrome. In: Harden R, Baron R, Janig W, eds. *Complex Regional Pain Syndrome.* Seattle, Wash: IASP Press; 2001.
33. Schurmann M, Gradl G, Andress HJ, Furst H, Schildberg FW. Assessment of peripheral sympathetic nervous function for diagnosing early post-traumatic complex regional pain syndrome type I. *Pain.* 1999;80:149-159.
34. Kemler MA, de Vet HC. Health-related quality of life in chronic refractory reflex sympathetic dystrophy (complex regional pain syndrome type I). *J Pain Symptom Manage.* 2000;20:68-76.
35. Carlson L, Watson H. Treatment of reflex sympathetic dystrophy using the stress-loading program. *J Hand Ther.* 1988;4:149-153.
36. Weber M, Birklein F, Neundorfer B, Schmelz M. Facilitated neurogenic inflammation in complex regional pain syndrome. *Pain.* 2001;91:251-257.
37. Fialka V, Korpan M, Saradeth T, et al. Autogenic training for reflex sympathetic dystrophy: a pilot study. *Complement Ther Med.* 1996;4:103-105.
38. Barowsky EI, Zweig JB, Moskowitz J. Thermal biofeedback in the treatment of symptoms associated with reflex sympathetic dystrophy. *J Child Neurol.* 1987;2:229-232.
39. Alioto JT. Behavioral treatment of reflex sympathetic dystrophy. *Psychosomatics.* 1981;22:539-540.
40. Blanchard EB. The use of temperature biofeedback in the treatment of chronic pain due to causalgia. *Biofeedback Self Regul.* 1979;4:183-188.
41. Kawano M, Matsuoka M, Kurokawa T, Tomita S, Mizuno Y, Ueda K. Autogenic training as an effective treatment for reflex neurovascular dystrophy: a case report. *Acta Paediatr Jpn.* 1989;31:500-503.
42. Gainer MJ. Hypnotherapy for reflex sympathetic dystrophy. *Am J Clin Hypn.* 1992;34:227-232.
43. Oerlemans HM, Oostendorp RA, de Boo T, Goris RJ. Pain and reduced mobility in complex regional pain syndrome I: outcome of a prospective randomised controlled clinical trial of adjuvant physical therapy versus occupational therapy. *Pain.* 1999;83:77-83.
44. Oerlemans HM, Oostendorp RA, de Boo T, van der Laan L, Severens JL, Goris JA. Adjuvant physical therapy versus occupational therapy in patients with reflex sympathetic dystrophy/complex regional pain syndrome type I. *Arch Phys Med Rehabil.* 2000;81:49-56.
45. Sherry DD, Wallace CA, Kelley C, Kidder M, Sapp L. Short- and long-term outcomes of children with complex regional pain syndrome type I treated with exercise therapy. *Clin J Pain.* 1999;15:218-223.
46. Lee BH, Scharff L, Sethna NF, et al. Physical therapy and cognitive-behavioral treatment for complex regional pain syndromes. *J Pediatr.* 2002;141:135-140.
47. Wilder RT, Berde CB, Wolohan M, Vieyra MA, Masek BJ, Micheli LJ. Reflex sympathetic dystrophy in children. Clinical characteristics and follow-up of seventy patients. *J Bone Joint Surg Am.* 1992;74:910-919.
48. Wesdock KA, Stanton RP, Singsen BH. Reflex sympathetic dystrophy in children. A physical therapy approach. *Arthritis Care Res.* 1991;4:32-38.
49. Moseley GL. Graded motor imagery is effective for long-standing complex regional pain syndrome: a randomised controlled trial. *Pain.* 2004;108:192-198.
50. Evans S, Fishman B, Spielman L, Haley A. Randomized trial of cognitive behavior therapy versus supportive psychotherapy for HIV-related peripheral neuropathic pain. *Psychomatics.* 2003;44:44-50.

51. Carlson CR, Hoyle RH. Efficacy of abbreviated progressive muscle relaxation training: a quantitative review of behavioral medicine research. *J Consult Clin Psy.* 1993;61:1059-1067.
52. Stetter F, Kupper S. Autogenic training: a meta-analysis of clinical outcome studies. *Appl Psychophysiol Biofeedback.* 2002;27(1):45-98.
53. Holroyd KA, Penzien DB. Pharmacological versus non-pharmacological prophylaxis of recurrent migraine headache: a meta-analytic review of clinical trials. *Pain.*1990;42:1-13.
54. Crider AB, Glaros AG. A meta-analysis of EMG biofeedback treatment of temporomandibular disorders. *J Orofac Pain.* 1999;13:29-37.
55. Malone MD, Strube MJ, Scogin FR. Meta-analysis of non-medical treatments for chronic pain. *Pain.* 1988;34:231-244.
56. Bogaards MC, ter Kuile MM. Treatment of recurrent tension headache: a meta-analytic review. *Clin J Pain.* 1994;10:174-190.
57. Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. *Pain.* 1999;80:1-13.
58. Rossy LA, Buckelew SP, Dorr N, et al. A meta-analysis of fibromyalgia treatment interventions. *Ann Behav Med.* 1999;21:180-191.
59. Astin JA, Beckner W, Soeken K, Hochberg MC, Berman B. Psychological interventions for rheumatoid arthritis: a meta-analysis of randomized controlled trials. *Arthritis Rheum.* 2002;47:291-302.
60. Sim J, Adams N. Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia. *Clin J Pain.* 2002;18:324-336.
61. Devine EC. Meta-analysis of the effect of psychoeducational interventions on pain in adults with cancer. *Oncol Nurs Forum.* 2003;30:75-89.
62. Eccleston C, Morley S, Williams A, Yorke L, Mastroyannopoulou K. Systematic review of randomised controlled trials of psychological therapy for chronic pain in children and adolescents, with a subset meta-analysis of pain relief. *Pain.* 2002;99:157-165.
63. Vlaeyen JW, Seelen HA, Peters M, et al. Fear of movement/(re)injury and muscular reactivity in chronic low back pain patients: an experimental investigation. *Pain.* 1999;82:297-304.
64. Asmundson GJ, Norton PJ, Norton GR. Beyond pain: the role of fear and avoidance in chronicity. *Clin Psychol Rev.* 1999;19:97-119.
65. Haythornthwaite JA, Clark MR, Pappagallo M, Raja SN. Pain coping strategies play a role in the persistence of pain in post-herpetic neuralgia. *Pain.* 2003;106:453-460.
66. Andrasik F, Holroyd KA. Specific and nonspecific effects in the biofeedback treatment of tension headache: 3-year follow-up. *J Consult Clin Psychol.* 1983;51:634-636.
67. Blake H. Strain and psychological distress among informal supporters of reflex sympathetic dystrophy patients. *Disabil Rehabil.* 2000;22:827-832.

TABLE 1. STUDIES EXAMINING PSYCHOLOGICAL/BEHAVIORAL INTERVENTIONS FOR CRPS

Author	Design and Sample	Psychological Intervention	Outcome
Blanchard (1979)[40]	Case Report n = 1 adult	Thermal biofeedback	Complete resolution of symptoms
Alioto (1981)[39]	Case Report n = 2 adult and adolescent	Autogenic and breathing relaxation, thermal and muscular biofeedback	75-100% reduction in pain
Barowsky et al (1987)[38]	Case Report n = 1 child	Thermal biofeedback	Complete resolution of symptoms
Kawano et al (1989)[41]	Case Report n = 1 adolescent	Autogenic relaxation, imagery	Complete resolution of symptoms
Wesdock et al (1991)[48]	Case Series n = 36 child and adolescent	Biofeedback	Helpful in some cases, particularly in CRPS of shorter duration
Gainer (1992)[42]	Case report n = 3 adult	Hypnotic imagery, relaxation training	Complete resolution of symptoms
Wilder et al (1992)[47]	Case Series n = 70 child and adolescent	Multidisciplinary treatment including relaxation training and CBT	Significantly improved pain and function in 57% of patients
Fialka et al (1996)[37]	Randomized Trial n = 18	PT (n=9), PT+ autogenics (n = 9)	Pain improved in both groups equally. Skin temperature more improved in autogenics group.
Sherry et al (1999)[45]	Case series n = 103 child and adolescent	Multidisciplinary treatment including psychotherapy for 77% of sample	Complete symptom resolution in 92% of sample at end of treatment, 88% symptom-free at 2 year follow-up
Oerlemans et al (1999; 2000)*[43,44]	Randomized Trial n = 135 adult	PT including relaxation training and cognitive interventions (n=44), OT (n = 44), Social Work Control (n=47). All patients received standard medical care.	Significantly greater improvements at 1 year follow-up for PT group than Controls on pain, temperature, active range of motion, and overall impairment scores
Lee et al (2002)[46]	Randomized Trial of Physical Therapy n = 28 child and adolescent	PT 1 X week + CBT (n=14), PT 3 X week + CBT (n = 14)	Pain and function improved significantly pre-post for both groups. Recurrence rate = 50%.

Note: Studies are listed in order of date of publication.
CBT = Cognitive-Behavioral Therapy, PT = Physical Therapy, OT = Occupational Therapy.
*Both Oerlemans et al studies were based on same sample.

FIGURE 1. PSYCHOLOGICAL INTERVENTION TREATMENT ALGORITHM.