Abbreviated Title: ACT Therapy for NF1Related Pain

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Title: Acceptance and Commitment Training for Adolescents and Adults with Neurofibromatosis Type 1, Plexiform Neurofibromas, and Chronic Pain: A Phase III Clinical Trial

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PRÉCIS

Background:

- Neurofibromatosis type 1 (NF1) is a genetic disorder that affects approximately 1 in 3,500 individuals.
- A number of common clinical manifestations, including plexiform neurofibromas, can cause frequent and significant pain and impact quality of life.
- Often, NF1-related pain is not well-controlled with medication and many of the medications cause significant side effects.
- To our knowledge, only one prior study (by our group) has examined the effectiveness of a psychological intervention for chronic pain in adolescents and young adults (AYA) with NF1.
- Acceptance and Commitment Therapy (ACT), a “newer generation” of cognitive-behavioral therapy, focuses on encouraging individuals to engage in more adaptive ways of coping with pain.
- The goal of ACT is not to eliminate the person’s pain, but to optimize the person’s functioning despite their pain.

Objective:

- To compare pain interference mean score changes from baseline to 8 weeks between the ACT intervention group and the waitlist (WL) group.

Eligibility:

- Patients 16 – 59 years of age with a confirmed diagnosis of NF1 and $\geq$1 plexiform neurofibroma (PN).
- The patient must obtain a mean score of 2.0 or higher or a score of 3 on three or more items on the Pain Interference Index, and report having pain that interferes with functioning for at least three months.
- The patient must have regular access to a computer or tablet with internet access.

Design:

- This is a psychological intervention study to determine the potential benefit of ACT on pain interference, with patients randomized to the ACT intervention or a wait-list control group.
- Patients will come to the NIH for a 2-day visit (Time 1). After baseline assessments (questionnaires and ECG) are completed, participants in the ACT group will take part in two 2-hour ACT training sessions. At home, this group will receive weekly emails through week 8, and will participate in further ACT training/educational sessions via video chat at weeks 2, 4, and 6.
- All patients will return to the NIH at week 8 (Time 2) to complete follow-up questionnaires and ECG. At this time, the WL group will cross over and receive the ACT intervention (in-person sessions, weekly emails, and video chat sessions). All patients will complete questionnaires again from home six months following the completion of the intervention.
- To detect a change of .68 standard deviation on the primary outcome measure between the two groups at .80 power, 41 patients per group are needed.

TABLE OF CONTENTS

1 INTRODUCTION

1.1 STUDY OBJECTIVES

1.1.1 Primary Objective

1.1.1.1 To evaluate whether patients receiving an Acceptance and Commitment Training (ACT) intervention demonstrate improved outcomes on a measure of pain interference (Pain Interference Index) when compared to a wait-list comparison group from baseline to 8 weeks (immediately post-intervention) in adolescents, and adults with NF1 and PNs who experience chronic pain that interferes with daily functioning.

1.1.2 Secondary Objectives

1.1.2.1 To examine baseline to 8-week changes in disease-specific quality of life, pain severity, pain-related anxiety, depression, and heart rate variability in patients receiving the ACT intervention.

1.1.2.2 To examine between-group differences in disease-specific quality of life, pain severity, pain-related anxiety, depression, and heart rate variability from baseline to 8 weeks.

1.1.2.3 To examine patterns of change from baseline to 8 weeks to 32 weeks in all primary and secondary outcome measures.

1.1.2.4 To examine potential mediators between pre- and post-treatment pain interference, including pain acceptance, psychological flexibility, as well as cognitive diagnosis (ADHD, LD), disease characteristics (stable vs. progressive disease, location of plexiform neurofibroma), and recent life events to determine whether these variables influence the effectiveness of the intervention.

1.1.2.5 To compare the reliability and validity of the two pain interference measures: the Pain Interference Index (PII) and the PROMIS Pain Interference scale.

1.2 BACKGROUND AND RATIONALE

1.2.1 Pain in Neurofibromatosis Type 1 (NF1)

Neurofibromatosis type 1 (NF1) is a genetic disorder caused by a mutation on chromosome 17 and affects approximately 1 in 3,500 individuals (Tonsgard, 2006). The disease is an autosomal dominant condition, and about half of cases arise from spontaneous mutations. Males and females are equally represented (North, 2000). Many patients are diagnosed during the first year of life, often due to the presence of café au lait macules. Typically, the frequency and severity of symptoms increases with age. The clinical presentation varies considerably, within and between patients (Rieley et al., 2011). Symptoms and complications include plexiform neurofibromas (PNs), café au lait spots, optic pathway gliomas, short stature, Lisch nodules, scoliosis, malignant peripheral nerve sheath tumors (MPNSTs), as well as cognitive deficits, learning disabilities, and social-emotional problems (Hyman, Shores, & North, 2006; Tonsgard, 2006).

Several clinical manifestations of NF1 can cause associated pain. Most importantly for this study, PNs are benign tumors comprised of a proliferation of cells in the nerve sheath (Friedrich, Schmelzle, Hartmann, Funsterer, & Mautner, 2005; Gutmann et al., 1997). Present in 30 to 50% of patients with NF1, PNs often exhibit rapid growth during childhood and adolescence but can occur at any age (Dombi et al., 2007; Tucker et al., 2009). These tumors can be internal without any visible indications, or they can be external and notably disfiguring. Further, PNs often cause significant pain that interferes with functioning (Kim et al., 2009; Wolters et al., in press), and negatively impact quality of life (QOL) (Wolkenstein et al., 2009).

While this protocol will include only individuals with PNs, these patients may have co-existing symptoms that cause pain in NF1, such as headaches (DiMario & Langshur, 2000), scoliosis and its treatments (Jett & Friedman, 2010; Weiss, 2003), pseudoarthrosis (Georgescu et al., 2007; Tonsgard, 2006), glomus tumors (benign tumors of the fingers and toes; (Brems et al., 2009)), and gastrointestinal complications (Heuschkel, Kim, Korf, Schneider, & Bousvaros, 2001).

The various conditions and symptoms described above emphasize the difficulties experienced by patients with NF1. Not surprisingly, more severe symptoms, including pain, were associated with worse QOL among 170 adults with NF1 (Page et al., 2006). Similarly, a previous study by our group (Burns et al., 2011a) noted that more severe pain correlated with worse QOL in 54 children and adolescents with NF1 and PNs. Further, more severe pain was found among the children with at-risk or clinically significant levels of depression and anxiety. There are ongoing efforts to develop and investigate chemotherapeutic agents, a few of which are promising. However, at present the main treatment is surgical removal of the tumors, which is often complicated by the involvement of nearby nerve tissue, and tumor regrowth is common (Jett & Friedman, 2010). Symptoms can be managed with pain medication, including nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, and narcotics; however, many patients taking these medications experience side effects (Rainsford, 1999; Rodriguez et al., 2008; Swann, 2001) and continue to report pain (Burns et al., 2011a; Kim et al., 2009). While one study with adults examined a psychological intervention for patients with NF1, the study also included individuals with NF2 and schwannomatosis, and not all patients with NF1 had PNs (Vranceanu, Merker, Plotkin, & Park, 2014). In terms of adolescents with NF1 and PNs, only one psychological intervention (ACT) for pain coping has been conducted to our knowledge (Martin et al., manuscript accepted).

1.2.2 Acceptance and Commitment Therapy

1.2.2.1 General Overview

Acceptance and Commitment Therapy (ACT) is one of the newer generations of cognitive-behavioral therapy (CBT) that has been used successfully to treat individuals with pain. One of the core therapeutic foundations of ACT is mindfulness, which is defined as "nonjudgmental, moment-to-moment awareness" (Kabat-Zinn, 1990). A broad research base strongly supports the effectiveness of mindfulness-based techniques for the improvement of psychological functioning and amelioration of symptoms such as anxiety and depression (Chiesa & Serretti, 2011; Hofmann, Sawyer, Witt, & Oh, 2010). The effects of mindfulness have been shown to last for up to four years (Kabat-Zinn, Lipworth, Burney, & Sellers, 1986) and its practice significantly reduces the risk of relapse or recurrence, for example, among depressed patients (Piet & Hougaard, 2011; Teasdale et al., 2000). A review article concluded that participation in mindfulness-based programs aimed at reducing stress improves coping and QOL in medical populations (Merkes, 2010). Moreover, several studies have pointed to neurobiological changes, such as prefrontal activation and increases in gray matter concentration in the hippocampus, that occur over extended mindfulness practice (Chiesa & Serretti, 2010; Holzel et al., 2011).

ACT is a therapeutic model that has grown out of CBT traditions and the mindfulness literature. It focuses on encouraging individuals to gain psychological flexibility so they can engage in more adaptive ways of coping with emotional or physical pain. The underlying premise is that, in many situations, attempting to control one's pain or problems is futile and can lead to the individual focusing a huge amount of their energy on a useless endeavor. As opposed to traditional CBT, which attempts to change people's irrational or negative thoughts, ACT uses mindfulness to help people become aware of their thoughts and accept them without judgment. When people increase their awareness of their thoughts, they are able to change their relationship with those thoughts, and not let the thoughts dictate their behavioral response. When individuals learn that they do not have to act upon their thoughts, they can then re-focus their energy toward engaging in behaviors that are in line with their core values and thus lead a more fulfilling life (Hayes, Strosahl, & Wilson, 1999).

During the past decade, ACT techniques have been applied to a wide range of presenting problems such as depression (Forman, Herbert, Moitra, Yeomans, & Geller, 2007), Post-Traumatic Stress Disorder (Walser & Westrup, 2007), Obsessive-Compulsive Disorder (Twohig, Hayes, & Masuda, 2006), smoking cessation (Hernandez-Lopez, Luciano, Bricker, Roales-Nieto, & Montesinos, 2009) and pain (L. M. McCracken, Vowles, & Eccleston, 2004; Wicksell, Melin, Lekander, & Olsson, 2009a), all with promising results. The effectiveness of ACT has been demonstrated when the treatment was administered via weekly sessions (Masuda, Cohen, Wicksell, Kemani, & Johnson, 2011; Wicksell, Melin, & Olsson, 2007) and in 1- or 2-day group workshops (Bach & Hayes, 2002; Butryn, Forman, Hoffman, Shaw, & Juarascio, 2011; Dahl, Wilson, & Nilsson, 2004; Pearson, Follette, & Hayes, 2011). In addition, in 2011, ACT was classified as having "strong empirical support" by the United States Substance Abuse and Mental Health Services Administration (nrepp.samhsa.gov). It is currently the only psychological therapy to have earned that designation.

1.2.2.2 The Use of ACT with individuals with chronic pain

In using ACT to help individuals with chronic pain, the goal is not to eliminate the person's pain, but to help the person achieve and maintain a high QOL while living with their pain. More specifically, patients are taught to notice their thoughts about their pain from a more neutral perspective, without necessarily acting upon them. Patients are then encouraged to consider their individual values and the way in which pain is interfering with leading a values-consistent life. For example, a patient may place a high value on their education, but may not spend as much time studying or attending classes as they would like due to their pain. They may have the thought "I have too much pain to go to class today," and then consequently avoid the associated behavior (i.e., going to class). When a person learns to notice those thoughts through mindfulness and related processes, they can then respond to those thoughts in accordance with their values while accepting the fact that they may experience pain in the process (e.g., go to class despite the pain).

Researchers have produced numerous studies supporting the effectiveness of ACT in individuals with chronic pain, including patients with severe debilitating pain (L. M. McCracken, MacKichan, & Eccleston, 2007). One study (Wicksell et al., 2013) randomly assigned women with fibromyalgia to an ACT intervention or a wait-list control condition. After 12 weekly group sessions, participants in the ACT arm demonstrated significant improvements in pain-related functioning, self-efficacy, depression, and anxiety, compared to the control group. In similar studies, ACT has been compared to relaxation training and treatment as usual, with results favoring the ACT groups on measures of pain-related disability, pain acceptance, depression, and overall satisfaction with life (L. M. McCracken, Sato, & Taylor, 2013; Thorsell et al., 2011).

It should be noted that some studies have found ACT to be comparable to CBT. In a study of 114 adults with chronic pain, including osteoarthritis and neuropathic pain, ACT was compared with traditional CBT over eight weeks of small group sessions (Wetherell et al., 2011). Results indicated significant improvements over time on pain interference, depression, and pain-related anxiety in both the ACT group and the CBT group. While there were no differences between the two groups on any of the primary outcome measures, participants in the ACT group reported a higher level of satisfaction with treatment at the end of the intervention. Overall, ACT is considered at least as effective as, and sometimes superior to, traditional therapies.

The use of ACT with individuals with chronic pain also has important implications for healthcare costs. Researchers in Sweden (Dahl et al., 2004) examined the effects of an ACT intervention on usage of sick leave and medical resources among public health employees considered at-risk for chronic pain and medical leave. Participants were randomized to receive four 1-hour sessions of ACT plus usual medical treatment, or usual medical treatment only. In the six months following the intervention, the ACT group utilized fewer sick days and fewer medical treatment resources than the comparison group. No pre-post differences were seen in QOL among either group. However, these results point to the potential for ACT to have a widespread economic impact.

ACT also has demonstrated effectiveness with adolescents with chronic pain. For example, one study (Wicksell et al., 2009a) utilized an ACT intervention with children and adolescents with long-term idiopathic pain. The children participated in ten weekly 1-hour sessions, and their parents participated in one to two 90-minute sessions. A comparison group of patients received a multidisciplinary treatment consisting of relaxation and imagery techniques, physiotherapy, and amitriptyline. Patients in the ACT group showed significant improvements from baseline to 3- and 6-month follow-ups in pain-related functioning according to both parent and child questionnaires. They also reported significantly less pain interference and better health-related QOL at follow-up. Compared to the multidisciplinary treatment group, the ACT group improved more with respect to pain impairment beliefs, pain intensity, and pain-related discomfort. The ACT group also showed less depressive symptoms at follow-up than the comparison group, although this difference was not statistically significant.

Finally, in 2011 a meta-analysis examined the effectiveness of ACT and other mindfulness-based interventions (collectively) among 19 studies of patients with chronic pain (Veehof, Oskam, Schreurs, & Bohlmeijer, 2011). Moderate, significant effect sizes were found for the impact of ACT on pain intensity, depression, anxiety, and QOL. The authors concluded that ACT has positive effects on physical and mental health among patients with chronic pain, and they cite the need for more scientifically sound studies to further this area of research.

1.2.2.3 Mediators of Treatment Efficacy

Recent publications have called for psychological intervention studies to include an examination of process variables, or the factors that may mediate the effectiveness of the intervention. The two process variables thought to be most relevant to ACT and chronic pain are pain acceptance and psychological flexibility. Acceptance of pain refers to a person’s willingness to live with their pain as opposed to taking the stance that their pain must remit before they can live their life (L. McCracken & Zhao-O'Brien, 2010). In a study of adults with chronic pain, researchers determined that changes in acceptance following an ACT intervention accounted for unique variance on all outcome measures, including pain-related disability, depression, anxiety, and performance on a timed-walk task (Baranoff, Hanrahan, Kapur, & Connor, 2013). Further, in adults with HIV disease and chronic pain, increases in pain acceptance during a 12-week ACT intervention were correlated with decreased pain-related impairment (Huggins, Bonn-Miller, Oser, Sorrell, & Trafton, 2012).

With respect to psychological flexibility as a process variable, Wicksell, et al. showed that the effectiveness of an ACT intervention in patients with chronic pain was mediated by variables consistent with psychological flexibility (Wicksell, Olsson, & Hayes, 2011). Vowles and McCracken (2010) examined effects of an ACT treatment on measures such as depression, anxiety, and physical functioning. They found that changes in psychological flexibility accounted for significant variance in most outcomes, while changes in more traditional pain management processes (e.g., distraction, relaxation, physical exercise) did not. The authors suggest that psychological flexibility should be considered as central to future investigations of chronic pain and relevant interventions (Vowles & McCracken, 2010).

1.2.2.4 Internet-delivered ACT

In recent years, mental health interventions have increasingly explored technological methods of delivery. Researchers are administering psychological treatments via email, online therapeutic materials, and smartphone applications with encouraging findings (Espie et al., 2012; Kirkpatrick, Manoukian, Dear, Johnston, & Titov, 2013; Swendeman, Comulada, Ramanathan, Lazar, & Estrin, 2014). In line with recommendations from a 2012 review article (Leykin et al., 2012), several studies have implemented ACT interventions via the internet. For example, one study randomized chronic pain outpatients to participate in seven weeks of an internet-guided ACT treatment or an online discussion forum about chronic pain (Buhrman et al., 2013). Findings were in favor of the ACT group on measures of pain interference, pain acceptance, anxiety, depression, and catastrophizing, with effects maintained six months post-treatment. Another study randomly assigned participants with chronic pain to an internet-guided ACT intervention, an online expressive writing intervention, or a wait-list control condition (Trompetter et al., 2014). Again, ACT group participants generally showed superior improvements on measures of pain interference, depression, and pain-related disability.

Video chat sessions have been utilized in a small number of studies involving individuals with medical conditions. These studies have been aimed at, for example, reducing sedentary behavior among individuals with multiple sclerosis (Klaren, Hubbard, & Motl, 2014) and increasing adherence among adolescents with poorly controlled diabetes (Freeman, Duke, & Harris, 2013). In addition, video chat was used in a recent study investigating effectiveness of an acceptance-based therapy similar to ACT, and the intervention was rated as feasible by the participants and therapists (Yuen et al., 2013). Technologies such as these are rapidly becoming common modes of administering psychological interventions among a wide variety of patient populations. However, video chatting has not been used in any published studies including patients with NF1.

1.2.2.5 Heart Rate Variability

The interaction between neural structures involved in pain perception and automatic nervous system (ANS) function are central to the process of pain regulation (Benarroch, 2006). Heart rate variability (HRV) is a physiological marker that has been used in numerous studies investigating

ANS pain reactivity. HRV refers to the sequence of time intervals between heart beats. Typically this is assessed via electrocardiogram (ECG), whereby the low-frequency (LF) HRV, high-frequency (HF) HRV, and low-to-high frequency ratio (LF/HF) are used as indices, depending on the research question. Greater HRV has been associated with better self-regulatory capacity (Reynard, Gevirtz, Berlow, Brown, & Boutelle, 2011; Segerstrom & Nes, 2007) and decreased sensitivity to experimentally-induced pain (Appelhans & Luecken, 2008).

In addition to changes seen in response to acute pain, chronic pain can result in long-term decreases in HRV. For example, individuals with complex regional pain syndrome (CRPS) have been found to have reduced HRV compared with healthy participants, which the authors noted to be consistent with "a general autonomic imbalance in cardiovascular regulation" (Terkelsen et al., 2012). In patients with musculoskeletal pain conditions, HRV was correlated with longer sick leave (Kristiansen et al., 2011). Among children and adolescents with chronic pain, HRV is significantly lower than healthy youth (Evans et al., 2013). Moreover, HRV has demonstrated sensitivity to change following medical (Jiang et al., 2011; Stein, Dal Lago, Ferreira, Casali, & Plentz, 2011) and psychological (Berry et al., 2014; Howorka et al., 2013) interventions. One study examined the relationship between anxiety symptoms and HRV among individuals randomly assigned to an ACT or CBT intervention (Davies, Niles, Pittig, Arch, & Craske, 2015); all participants had been diagnosed with an anxiety disorder. HRV was found to predict outcomes on an anxiety symptom questionnaire in both groups, such that patients with low baseline HRV improved more than those with high baseline HRV. The authors suggest that ACT and CBT may be most effective for people with lower HRV (such as those with chronic pain, typically).

A recent review article (Koenig, Jarczok, Ellis, Hillecke, & Thayer, 2013) summarized the research on HRV across pain conditions. The authors noted that HRV is a physiologically grounded, theoretically sound and empirically-supported index that should be considered as an outcome measure for interventions targeting pain relief. Further, the knowledge gained from studies of HRV "may have important clinical implications [for] a large variety of health conditions" (Koenig, et al., page 312).

1.2.2.6 Preliminary Data

In a recent pilot study by our group, twelve adolescents (6 males) with NF1 and PNs and their parents completed a 2-day ACT workshop (*M* age = 16.9 years), with 10 patients and 7 parents providing 3-month follow-up data. Pre-post comparisons showed that patients and parents reported that pain interfered significantly less with the adolescents' daily lives at three months ($ps<.05$). Additionally, patient-reported pain intensity on a 100-mm visual analogue scale significantly declined from baseline to three months (baseline $M = 43.0$, 3-month $M = 29.3$; $p<.05$). Parents reported marginally greater acceptance of their child's pain ($p=.07$). No changes were seen in functional ability or mood. Thus, preliminary findings suggest that an ACT intervention has potential as a non-pharmacological method for helping individuals with NF1 and PNs (Martin et al., manuscript accepted).

1.2.3 Rationale for the Proposed Study

Overall, the research on ACT to date indicates that it is as helpful as, or superior to, other methodologies (e.g., treatment as usual, traditional CBT, relaxation) for individuals with various types of pain. Thus, it is plausible that it would be helpful to patients with NF1. However, no randomized studies have investigated the use of behavioral interventions for pain in the NF1 population, despite the need for such therapies. Because pharmacologic treatments do not always eliminate painful symptoms (Burns et al., 2011b) and can cause unpleasant side effects (Swann, 2001), these options are not always ideal. Members of our NF1 research team conducted a survey of parents with a child with NF1 who was evaluated at the NCI for a clinical trial (Martin, Gillespie, Wolters, & Widemann, 2011). Results indicated that 63% of respondents expressed interest in future studies investigating pain. Establishment of a successful intervention targeting chronic pain in NF1 would be a critical step forward in improving the functioning and QOL of these patients.

Since previous studies have suggested that both in-person and internet-delivered ACT interventions are efficacious, the proposed study will implement an ACT intervention through two, 2-hour in-person sessions and online follow-up with adolescents and young adults with NF1 and PNs who experience chronic pain. We chose to use a slightly older age group than our pilot study; while the small number of patients in that study prohibited statistical analysis of different age groups, our clinical experience suggested that the younger adolescents had more difficulty understanding some of the concepts. A randomized study design is warranted based on previous literature supporting ACT's efficacy including our own preliminary data in patients with NF1, and because the two-group comparison design will allow us to establish whether patients improve more with ACT compared to patients doing their usual strategies to manage pain. Moreover, this design will allow for all participants to receive the intervention. The in-person plus internet format was chosen due to the infeasibility of conducting regularly-scheduled sessions with patients who live long distances from the NIH and because frequent out-of-home sessions are often unrealistic due to time or financial constraints. Finally, it should be mentioned that a notable proportion of individuals with NF1 have learning or attention deficits (Hyman et al., 2006). We do not expect this to pose a problem, since ACT and related therapies have demonstrated efficacy among individuals with developmental delays and attention problems (Robertson, 2011; Zylowska et al., 2008). While we will screen out prospective participants with significant cognitive deficits, we also made a number of modifications to the manual and workbook from our pilot study to make the intervention more appropriate for individuals with minor cognitive impairments, e.g., ADHD. For example, we eliminated exercises with more abstract metaphors and made several of the assignments more detailed and with more specific instructions. In addition, extending the intervention so that we maintain regular contact over 8 weeks hopefully will enable us to keep less focused individuals on track.

1.2.4 General Overview

The proposed study will use a randomized controlled trial design to compare the treatment group (Acceptance and Commitment Training; ACT) to a wait-list group (WL) in adolescents and young adults ages 16 – 59 years with NF1 and PNs who report chronic pain. Patients will be recruited from Dr. Brigitte Widemann's NF1 program at the National Cancer Institute, from NF1 clinics around the country, and via the Children's Tumor Foundation (CTF) registry. With all patients, we will implement an 8-week in-person and internet-delivered ACT intervention. All participants will complete their Time 1 assessment (ECG and questionnaires) on day 1 at the NIH before being randomized.

<u>Participants assigned to the ACT group</u> will meet with a trained ACT therapist for two in-person sessions at the NIH (days 1 and 2). Upon returning home, weekly emails will be sent to patients

for 8 weeks, each containing ACT-related information and exercises to complete at home. Video chat sessions will be conducted via computer at weeks 2, 4, and 6. These patients will return to the NIH at week 8 for their Time 2 assessment (repeat ECG and questionnaires). They will be encouraged to continue using ACT techniques in their daily lives. They will be sent follow-up questionnaires to complete electronically from home six months following completion of the 8-week intervention (week 32; Time 3).

Participants assigned to the WL group will return home after completing the Time 1 baseline assessment. They will return to the NIH at week 8 to complete Time 2 follow-up measures (ECG, questionnaires); these data will serve as the primary comparison with the ACT group and will also serve as their baseline assessment for the ACT arm. These participants will then receive the same ACT intervention as described above (two 2-hour in-person sessions, weekly emails, biweekly video chat sessions). They will return to the NIH after the 8-week ACT intervention (at about week 16) to repeat follow-up measures, and will then be encouraged to continue using ACT techniques in their daily lives. Six months later (week 40), they will complete questionnaires online from home. Thus, because they cross over to the ACT intervention after the wait-list period, participants in this group will complete the measures a total of 4 times (as opposed to 3 times in the ACT immediate intervention group).

At the completion of each visit or set of follow-up questionnaires, participants in both groups will receive a small amount of money ($30) to thank them for their time. The 8-week data will be the primary endpoint and analyses will be conducted to determine changes over time in ACT versus WL on the primary outcome measure (pain interference) and various secondary measures (outlined below). Forty-one patients per arm will provide 80% power to test the 0 to 8-week differences in changes from baseline between the two arms.

	Days 1-2	**Weeks 1-8**	**Week 8**	**Weeks 8-16**	**Week 16**	**Week 32**	**Week 40**
ACT	• Time 1 evaluations • In-person ACT sessions	• Weekly emails • Video chat weeks 2,4,6 (home)	• Time 2 evaluations (NIH)	Continue ACT practice (home)		Time 3 questionnaires (home)	
WL	• Time 1 evaluations		• Time 2 evaluations • In-person ACT sessions	• Weekly emails • Video chat weeks 2,4,6 (home)	Time 3 evaluations (NIH)	Continue ACT practice (home)	Time 4 questionnaires (home)

2 ELIGIBILITY ASSESSMENT AND ENROLLMENT

2.1 ELIGIBILITY CRITERIA

2.1.1 Inclusion Criteria for Participant

2.1.1.1 Patients must be between 16 and 59 years of age at the time of the baseline assessment. Because the research on the effectiveness of ACT with younger children is still emerging, children 15 and younger will be excluded from the present study.

2.1.1.2 Diagnosis of NF1 through germline mutation OR clinical diagnosis; for the clinical diagnosis of NF1 all study subjects must have two or more diagnostic criteria for NF1 listed below (NIH Consensus Conference):

1. Six or more café-au-lait spots (≥0.5 cm in prepubertal subjects or ≥1.5 cm in postpubertal subjects)
2. ≥ 2 neurofibromas or 1 plexiform neurofibroma
3. Freckling in the axilla or groin
4. Optic glioma
5. Two or more Lisch nodules
6. A distinctive bony lesion (dysplasia of the sphenoid bone or dysplasia or thinning of long bone cortex)
7. A first-degree relative with NF1

2.1.1.3 Participants must have documentation of a PN, based on either clinical exam or imaging.

2.1.1.4 Patient must self-report having chronic pain for at least the past 3 months that has interfered with their daily functioning, as assessed by the Pain Interference Index (must get a mean score of 2.0 or higher, or score a 3 on three or more individual items).

2.1.1.5 Patients must have regular access to a computer or tablet with internet access.

2.1.1.6 Ability of subject or Legally Authorized Representative (LAR) to understand and the willingness to sign a written informed consent document.

2.1.1.7 No anticipated major changes in their pain treatment regimen (i.e., new class of pain medication starting or change in the class of pain medication) or enrollment on a new treatment study presumed to impact pain in the near future.

2.1.1.8 Subjects must be able to read and comprehend the English language, since the highly trained ACT therapists are not fluent enough to conduct the trainings in Spanish or other languages.

2.1.2 Exclusion Criteria for Participant

2.1.2.1 In the opinion of the PI or an AI, the subject has significant cognitive or emotional difficulties that would prevent them from being able to understand and/or participate fully in the intervention or the measures.

2.1.2.2 Subjects who are participating in any other treatment studies, either medical or behavioral, specifically for pain management.

2.1.2.3 Subjects who began a medical intervention for treatment of their disease that has a possible impact on pain (including MEK trials) will not be eligible until after one year on the medical treatment; at that time, eligibility will be discussed with the PI of the medical study to assess the stability of the patient's pain and whether further pain-related changes due to the medical treatment are likely.

2.1.2.4 Inability to travel to the NIH, for example, due to physical limitations, for the in-person evaluation(s).

No groups in regards to gender, race, or ethnicity are being excluded from participation in the trial.

2.1.3 Recruitment Strategies

Dr. Widemann has an active clinical trials program for NF1 consisting of both natural history and treatment protocols for PNs and MPNSTs, which draws patients from a national referral base. All patients on Dr. Widemann's study who have reported moderate to severe pain to the medical team and are within the study's age range will be informed about the study unless they meet exclusion criteria. Subjects will be recruited from this referral base, as well as from medical centers around the country. We also plan to advertise the study in the Children's Tumor Foundation (CTF) newsletter and website, as well as the CTF Registry. There are some external funds available to assist with travel costs.

2.2 SCREENING EVALUATION

2.2.1 Pain level

Because it is not feasible to bring patients here from long distances for this protocol and then find them ineligible based on questionnaire responses, a screening questionnaire will be administered by study staff over the telephone prior to bringing potential subjects to NIH for the complete screening evaluation (See **Appendix A**).

The screening questionnaire consists of the 6-item Pain Interference Index (PII), which will be administered verbally, with the researcher reading the questions to them. We will ask each participant if they prefer to read the questions along with the researcher, in which case we will email the questions to them and then resume the call. To be found eligible, individuals must obtain a mean score of 2.0 or higher OR respond with a '3' or higher to three or more items. Patients will not be told in advance what PII score criteria they have to meet to be eligible. In addition, they must report that their pain has been present for at least the past three months. They also must confirm that they have access to a computer (or tablet or smartphone) with internet capability, and that they can read and speak standard English. Patients who meet these criteria and who are interested in participating will be brought to NIH for complete screening at which time they will be given a copy of the screening consent that has been reviewed; the consent will then be signed in the clinic. Patients who are already enrolled on Dr. Widemann's Natural History protocol may be approached in clinic or by phone or email and may be given the screening evaluation for the current study at that time if the patient expresses interest in learning about the study.

2.2.2 History and Physical Examination

Patients who meet the initial phone screening evaluation and who are interested in participating will meet with a nurse practitioner or physician for a history and physical examination at the NIH Clinical Center. This will include a complete history (including prior and concurrent treatments); physical examination including a neurological examination, documentation of performance status, blood pressure, and signs and symptoms of NF1, including a thorough history of pain experiences; and pain medications, doses, frequency, etc., and history of cognitive diagnoses (ADHD, LD). If the subject is co-enrolled on NCI protocol #08-C-0079 (Natural History Study and Longitudinal Assessment of Children, Adolescents, and Adults with Neurofibromatosis Type 1), the physical evaluation will not be repeated for this intervention study if obtained within 4 weeks of study entry, and the results may be included in the data analysis for this study. If a patient has been evaluated in the past 6 months for the Natural History Study, an abbreviated history and physical examination will be conducted, with a particular emphasis on recent pain history and pain management. No other medical screening procedures will be done.

2.3 REGISTRATION PROCEDURES

Registration will be a two-part process as patients are screened on this protocol. Authorized staff will register an eligible candidate with NCI Central Registration Office (CRO) within 24 hours of signing consent. To initially register a subject after the participant has signed the consent, complete the top portion of the registration Eligibility Checklist from the website (http://home.ccr.cancer.gov/intra/eligibility/welcome.htm) indicating that the patient is being registered for screening and sent via encrypted email to: NCI Central Registration Office ncicentralregistration-l@mail.nih.gov. Once eligibility is confirmed after completion of screening studies, complete the remainder of the form which is the eligibility checklist, indicating that the patient is being registered for treatment and email the completed registration checklist to the CRO at NCI Central Registration Office ncicentralregistration-l@mail.nih.gov. Verification of registration will be forwarded electronically via e-mail to the research team. A recorder is available during non-working hours.

Subjects that do not meet screening criteria should be removed from the study following the procedure in section **3.6**.

2.3.1 Treatment Assignment and Randomization/Stratification Procedures

2.3.1.1 Cohorts

Number	**Name**	**Description**
1	Patients	Patients diagnosed with NF1 through germline mutation OR clinical diagnosis

2.3.1.2 Arms

Number	**Name**	**Description**
1	ACT	ACT intervention
2	WL	Wait List Control Group

2.3.1.3 Stratifications

Name	**Distinct Options**	**Notes**
Age	16-24 years 25-59 years	

2.3.1.4 Randomization and Arm Assignment

All patients in cohort 1will be stratified for age and randomized between arms 1 and 2. After patients have been on the Wait List Arm for 8 weeks, they will cross over to the ACT arm.

2.4 BASELINE EVALUATION

After signing consent for participation in this study, the following baseline assessments will be conducted:

1. The following questionnaires will be required of all participants (See Section **3.3.1** for a complete description of these questionnaires):

Table of Questionnaires:

Domain	**Questionnaire Name**	**Location**	**Completion Time***
Demographics	Background Information Form	**Appendix B**	2 min
Pain Interference	Pain Interference Index PROMIS Pain Interference SF – Adult PROMIS Pain Interference SF – Pediatric	**Appendix C** **Appendix D** **Appendix E**	2 min 3 min 3 min
NF1 Quality of Life	PedsQL Neurofibromatosis Type 1 Module	**Appendix F**	5 min
Pain-related Anxiety	Pain Anxiety Symptoms Scale-20 (PASS-20)	**Appendix G**	5 min
Depression	Center for Epidemiological Studies-Depression Scale (CES-D)	**Appendix H**	5 min
Pain Intensity	Numeric Rating Scale-11 (NRS-11)	**Appendix I**	1 min

Pain Acceptance	Chronic Pain Acceptance Questionnaire (CPAQ)	**Appendix J**	5 min
Psychological Inflexibility	Psychological Inflexibility in Pain Scale (PIPS)	**Appendix K**	3 min
Recent Life Events	Life Events Scale (LES)	**Appendix L**	1 min
Pain Management Strategies	Pain Management Inventory (PMI)	**Appendix M** **Appendix N**	2 min
ACT adherence	ACT Inventory**	**Appendix O**	
Subjective Overall Change	Patient Global Impression of Change scale (PGIC)**	**Appendix P**	1 min
Estimated Reading Ability	Wide Range Achievement Test – Fourth Edition (WRAT-4)	not shown	2 min

* Total time required for patients: about 32 – 37 minutes at each time point.
** The ACT Inventory and PGIC scales are given at follow-up time points only.

2. Electrocardiogram: a baseline ECG will be performed on all patients. The ECG will be administered in a room in the Pediatric clinic by a trained member of the research group (see section **3.3.2**).
3. Imaging (optional): We will examine prior scans of patients' plexiform tumor *if available*. We will not perform imaging as part of the current study. If patients have a prior scan taken within one year of beginning this study, we will use this to document location of the PN. If two prior scans are available taken approximately 1 – 2 years apart, we will use these to determine if the PN is stable vs. progressive. We will ask patients who have scans from an outside institution to have them mailed to Eva Dombi, NCI Pediatric Oncology Branch, 10 Center Drive, Building 10, room 1-5750, Bethesda, MD, 20892, or dombie@mail.nih.gov.

3 STUDY IMPLEMENTATION

3.1 STUDY DESIGN

3.1.1 Baseline

On Day 1 after signing consent, participants will be randomized to their group as described above (section**2.3.1.4**). All patients will receive an electrocardiogram (ECG) to assess HRV and will be asked to complete a baseline demographic questionnaire and nine baseline questionnaires. The brief demographic questionnaire asks about level of independence, occupation and educational history, and history of psychiatric diagnoses. This form should take about 5 minutes to complete. The other nine baseline questionnaires should take 30-35 minutes total. The patient will also take a 1- to 2-minute word reading test as an estimate of reading ability. Following these baseline procedures, patients will be informed of their randomized group assignment.

Patients who are assigned to the ACT group will meet with their assigned trainer for Session 1, typically that same day, and will take part in Session 2 typically the following morning. One 5-

10 minute break will be given during each 2-hour session (see Section **3.2.2** for more information on the content of these sessions). At the end of the Day 2 ACT session, patients will be given materials to take home so they may continue to practice ACT techniques in their daily lives. These include a workbook (see **Appendix Q**) and an audio CD or MP3 download with mindfulness exercises focused on pain. We anticipate that most patients in the ACT group will be able to return home on Day 2, depending on travel arrangements.

Patients assigned to the WL group will return home after the baseline questionnaires and ECG are completed. Thus, their total stay at the NIH will be less than 1 day for local patients, and 1 to 1.5 days for patients traveling long distance.

Participants in the ACT group will receive weekly emails with a different topic and practice exercise each week (**Appendix R**), and will participate in biweekly, individual video chat sessions with their assigned trainer. This will be the same trainer who conducted their in-person sessions, whenever possible (e.g., unless that trainer is out sick for an extended period). These sessions will be scheduled to last about 30 minutes each. See **Appendix S** for the video chat manual.

3.1.2 Follow-up

Participants in both groups will return to the NIH at the end of the 8-week intervention (not to exceed 12 weeks after their initial NIH visit). During this visit, all participants will repeat the baseline evaluations: they will complete follow-up questionnaires as listed in section **2.4** and will have a second ECG. After those evaluations, the ACT participants will return home with instructions to continue using the ACT techniques in their daily lives. The WL participants will then receive the 2-session in-person ACT intervention (typically over two days), and then will return home to take part in the weekly emails and individual video chat sessions.

At the end of their 8-week intervention, participants in the WL group will return to the NIH for their final in-person visit when they will complete the follow-up questionnaires again and will receive their final ECG. If it is a hardship for patients in the WL group to return for a third visit (i.e., for those who live across the country), they will be given the option to complete the questionnaires online from home. Thus, we will have questionnaire data for these patients but will forego their second follow-up ECG data.

Both groups will complete a final set of questionnaires from their home computer, tablet, or smartphone about six months (about 24 weeks) after the formal intervention ends.

3.2 ACT INTERVENTION

3.2.1 Therapist Training

The ACT training sessions (in-person and video chat) will be led by one of four therapists: Dr. Staci Martin Peron, who is a licensed psychologist, Dr. Kari Struemph (licensed psychologist), Mary Anne Tamula, MA (Psychology Associate), or another Psychology Associate (probably a post-doctoral fellow) to be hired for this study; this person will see the majority of patients. All sessions led by the Psychology Associates will be supervised by Dr. Martin Peron. Dr. Martin Peron and Ms. Tamula have participated in formal ACT training, including attending numerous workshops with experts in the field, studying books and articles on ACT techniques, and attending a monthly peer consultation group. Dr. Martin Peron has given numerous talks on ACT for pain management, and has trained and supervised other psychologists, Psychology Associates, and psychology graduate students in this area. The other two therapists will participate in a local ACT training if one becomes available and will engage in structured training and supervision with Dr. Martin Peron. All therapists will complete the Acceptance and Commitment Therapy Core Competency Self-Rating Form (Hayes & Strosahl, 2004). To assess treatment fidelity, trainers will complete a checklist of techniques and intervention procedures after each in-person session (see **Appendix T**).

3.2.2 ACT Training Content

3.2.2.1 In-person ACT sessions

The in-person ACT sessions will consist of structured techniques focused on helping participants cope with their pain more effectively. The sessions will follow a manual that was adapted from our previous pilot study for groups of patients with NF-related pain; the format for the current study has been adapted for use with individuals. Content also was based on previous manualized ACT interventions outlined in books (Dahl, Wilson, Luciano, & Hayes, 2005; Hayes et al., 1999) and articles (Masuda et al., 2011; Wicksell, Dahl, Magnusson, & Olsson, 2005; Wicksell et al., 2007) and used in prior ACT studies with chronic pain patients.

The ACT manual is presented in **Appendix U**. In general, the content of the in-person and video chat sessions will be based on the six core therapeutic processes of ACT, each of which are interrelated and build upon the others:

(1) <u>Mindfulness.</u> Mindfulness is of central importance in ACT. Participants will be taught to practice mindfulness exercises to help them be aware of internal and external events as they occur. Engaging in mindfulness helps people become more aware of their automatic, maladaptive thoughts and be more flexible in their reactions to them. Basic mindfulness exercises, such as focusing on one's breathing or on particular sights or sounds, will help individuals learn to observe and describe these things in a neutral manner. Then the focus of mindfulness exercises will be extended to thoughts about the person's pain.

(2) <u>Acceptance.</u> Patients will be encouraged to be willing to experience their pain and the thoughts and feelings they have about their pain without judging or trying to change them. They will be taught to let go of their struggle against pain as a means of opening themselves up to more adaptive ways of living. One's willingness to experience pain can lead to the creation of a more full and vital life, since all the energy once spent avoiding pain can now be focused on valued activities and goals.

(3) <u>Cognitive Defusion.</u> Defusion refers to the process of separating the words people use from their literal meaning. For example, just because a patient has the thought "I can't stand this pain" does not make it true. Participants will be taught to observe their thoughts without necessarily believing them to be true or acting upon them. The therapist accomplishes this by labeling the person's thoughts as only thoughts rather than known facts. If a patient states "I can't go to the football game because my arm hurts" the therapist can reframe that as "You're having the thought that you can't go to the game" to emphasize that the statement may not be true. This gradually helps the people disentangle themselves from their thoughts, and frees them up to make choices based on factors other than the immediate thoughts they have about their pain.

(4) Self as Context. This aspect of ACT refers to helping participants become more aware of a sense of self from which they can observe and accept their thoughts, emotions, and experiences. Doing so helps individuals become disentangled from their maladaptive thoughts, since they are encouraged to experience them as an observer rather than a participant. This, in turn, helps the participant to view his or her struggle with more objectivity and compassion.

(5) Defining Valued Directions. Patients will participate in exercises aimed at helping them define their core values and then will examine the ways in which their current behaviors are interfering with their ability to live their life consistent with their values. The therapists will demonstrate how focusing on avoidance of pain means that one is not focusing on valued activities. Living in accordance with one's values and without pain may not be possible. This is an important point for patients to realize.

(6) Committed Action. Participants will be asked to define concrete goals that are consistent with their core values, and then commit to living in accordance with these goals. Potential barriers to reaching their goals will be addressed, with specific focus on how to respond when faced with obstacles. Therapists also will focus on how to engage the support of significant others (for example, parents, friends, spouses) in one's pursuit of his or her goals.

Participants will complete practice exercises on their own in between the two sessions. At the end of the second session, patients will be given a workbook to take home that includes a summary of the topics discussed during the sessions and exercises for continuing to work on ACT techniques at home. In addition, patients will be given an audio CD or MP3 download that contains mindfulness meditations geared towards individuals with chronic pain ("Mindfulness Meditation for Pain Relief" by Jon Kabat-Zinn).

3.2.2.2 Emails

Weekly emails will be sent to each ACT group participant during weeks 1 – 8 (see **Appendix Q**). These emails will contain a brief summary of a topic relevant to ACT concepts, and an exercise or assignment for the participant to complete that week. If the participant emails the trainer with a specific question, the trainer will respond as soon as possible (typically within 24 hours, not including weekends). Any medical questions will be referred to the patient's medical provider. The main content of the emails will be the same across patients, but certain examples in the emails may be adapted slightly depending on the patient's age or individual goals. For example, we may discuss a 16-year old patient's goal of doing well in school, or a 28-year old patient's goal of joining a book club.

3.2.2.3 Video chat Sessions

Each individual, 30-minute video chat session will be structured as follows (approximately): 5 minutes to review the topics from the weekly emails, 15 minutes to introduce a new topic (related to previous content), and 10 minutes to discuss any difficulties the patient may be experiencing in relation to their pain or the intervention exercises. The manual for video chat sessions is in **Appendix S**.

3.3 QUESTIONNAIRES

3.3.1 Patient Questionnaires

3.3.1.1 Pain Interference

The Pain Interference Index (PII) is a 6-item questionnaire meant to assess the degree to which pain has interfered with daily activities in the past week (**Appendix C**). This measure initially was developed and validated in Sweden with youth with longstanding idiopathic pain (Wicksell, Melin, Lekander, & Olsson, 2009b). In collaboration with the Swedish researchers, the authors of the current study translated the measure to English and also created a parallel parent report version (PII-P) and an adult self-report version. The youth self-report PII has been validated in patients ages 6 to 25 years with NF1 and other chronic illnesses (Martin et al., 2014). For this study, this version will be administered to patients ages 16 to 17 and to 18-25 year olds who are still in school. The adult self-report version is parallel to the youth self-report version, with minor wording modifications made (changing "school" to "work"). Initial reliability and validity data of the adult self-report version are positive (alpha = .94; manuscript in preparation). Both versions of the scale take about 2 minutes to complete.

The PROMIS Pain Interference scales will be administered as another assessment of pain interference (Appendices C and D); (Amtmann et al., 2010; Varni et al., 2014). The adult 8-item short form will be administered to participants ages 18 - 59, and the pediatric 8-item short-form will be given to participants ages 16 and 17 years. Both of these scales ask the respondent to consider how much pain has interfered with things like sleep, mood, and leisure activities, in the past week. Items are formatted on 0-4 Likert scales. These measures each take about 2 minutes to complete. The PII and the PROMIS pain interference scales are both being given since they each have advantages and disadvantages. Specifically, the PII's limited items may not capture all relevant aspects of pain interference in NF1, but this measure has strong preliminary reliability and validity data in this population, which the PROMIS does not yet have. Moreover, giving both measures in conjunction is the current recommendation of the Patient-Reported Outcomes (PRO) working group of the Response Evaluation in Neurofibromatosis and Schwannomatosis (REiNS) collaboration.

3.3.1.2 Disease-specific Quality of Life

The PedsQL NF Module, Adult form is a questionnaire designed to assess various aspects of quality of life in individuals with NF1 (Nutakki, Hingtgen, Monahan, Varni, & Swigonski, 2013) (**Appendix F**). Items on this scale ask the respondent to indicate the extent to which they have had problems performing various activities over the past month, using a 0 – 4 Likert scale (0 = Never, 4 = Almost Always). The subscales that will be administered on this study include Physical Functioning (7 items) and Daily Activities (12 items). Mean scores for each subscale are linearly transformed to a 0-100 scale, and then can be compared to means and standard deviations of a normative group of patients with NF1. These two subscales should take less than five minutes to complete.

3.3.1.3 Pain-related Anxiety

The Pain Anxiety Assessment Scale – 20 (PASS-20) is a 20-item measure developed to assess pain-related anxiety in medical patients (McCracken & Dhingra, 2002; see **Appendix G**). Items are answered on a 6-point Likert scale with anchors of "never" and "always." Responses provide a total score and scores on four subscales: Cognitive Anxiety, Pain-related Fear, Escape and Avoidance, and Physiological Anxiety. The PASS-20 is reliable (Cronbach's alpha = .81) and valid (L. M. McCracken & Dhingra, 2002; Roelofs et al., 2004). The measure takes about 5 minutes to complete.

3.3.1.4 Depression

The Center for Epidemiological Studies – Depression scale (CES-D) (Radloff, 1977) is a 20-item measure originally developed for use with individuals 18 years and older, and has since been validated with adolescents as young as 12 years (Garrison, Addy, Jackson, McKeown, & Waller, 1991). Respondents are asked to rate how frequently in the past week they have experienced a list of symptoms, such as feeling depressed, enjoying life, having problems sleeping, and feeling liked by people. Items are scored on a 0 (rare or none of the time) to 3 (most of all of the time) format. Individual responses yield scores on four subscales: depressive affect, positive affect, somatic activity, and interpersonal. A total depression score is obtained that can range from 0 to 60, with higher scores representing worse depressive symptoms. This tool has been shown to be valid and reliable in clinical populations (Orme, Reis, & Herz, 1986) and with medical patients, including those with chronic pain (Hann, Winter, & Jacobsen, 1999; Turk & Okifuji, 1994). This questionnaire takes approximately 5 minutes to complete (See **Appendix H**).

3.3.1.5 Pain Intensity

The Numeric Rating Scale – 11 (NRS-11) consists of two questions that assess pain intensity. The items are formatted along a horizontal line with from 0 (no pain) to 10 (worst pain imaginable) spaced equidistant along the line (**Appendix I**). Respondents circle the one number that best represents their pain currently, and in the past week. This measure is widely used and is recommended for use in clinical trials for patients with chronic pain, including NF1 (Wolters et al 2013; Gilron & Jensen, 2011). It takes less than one minute to complete.

3.3.1.6 Coping with Pain

The Chronic Pain Acceptance Questionnaire (CPAQ; (L. M. McCracken et al., 2004) was designed to assess one's ability to accept his or her pain, and is typically used with patients ages 18 years and older. Respondents answer 20 questions on a 0 (never true) to 6 (always true) rating scale, with higher scores indicating higher levels of acceptance. Scores are obtained on two subscales (Activities Engagement and Pain Willingness) and an Acceptance Total scale. Reliability and validity, and sensitivity to change have been demonstrated (Huggins et al., 2012; Vowles & McCracken, 2008). The CPAQ takes approximately 5 minutes to complete (See **Appendix J**).

3.3.1.7 Psychological Inflexibility

The Psychological Inflexibility in Pain Scale (PIPS) is a 12-item measure that assesses the extent to which an individual engages in avoidance of activities because of their pain (experiential avoidance) and inflexible thinking about their pain (cognitive fusion) (Wicksell, Lekander, Sorjonen, & Olsson, 2010); **Appendix K**). The measure asks respondents to rate how true the statements are for them currently, on a Likert scale of 1 (never true) to 7 (always true). Eight of the items are summed to yield a score on the Avoidance subscale, and four of the items are summed for the Fusion subscale. A total score also is obtained by summing all 12 items. The PIPS has been found to have good internal consistency and strong correlations with criterion variables such as pain intensity, use of pain medication, and other measures of activity avoidance (Trompetter et al., 2014; Wicksell et al., 2010). The form takes about 3 minutes to complete.

3.3.1.8 Recent Life Events

Because stressful life events may impact pain and coping, we will administer the Life Events Scale (LES), a measure designed to assess significant events that have occurred in the patient's life in the past six months (**Appendix L**). The patient is asked to indicate which events have occurred in their life from a list of 43 potential events. This scale has shown reliability and validity (Elliott-Desorbo, Martin, & Wolters, 2009).

3.3.1.9 Pain Management

The Pain Management Inventory (PMI) was developed by our group to assess what techniques patients use to manage their pain, including pharmacological and non-pharmacological treatments. Specifically, respondents are asked what pain medications they have taken in the past month and how frequently. Another question asks about any other (non-pharmacological) techniques in which participants have engaged (e.g., relaxation, massage) for coping with pain in the past month. At the 6-month time point, there is an additional question on this form that asks whether the patient has had surgery for their NF1 in the past six months. This measure takes about 2 minutes to complete (see **Appendix M** and **Appendix N**).

3.3.1.10 Adherence to ACT Intervention

The ACT Inventory was developed by our group to assess the frequency with which participants have engaged in ACT strategies in the past month. Six items ask how much participants have used mindfulness, defusion, and other ACT techniques taught during the intervention to help them cope with pain in their daily lives. One item asks how much the person liked participating in the study. This will be given at follow-up time points only, and takes about 2 minutes to complete (see **Appendix O**).

3.3.1.11 Subjective Change Rating

The Patient Global Impression of Change (PGIC) scale is one item used to assess the patient's overall impression of their level of pain interference at the end of the study compared to baseline (see **Appendix P**). Versions of this scale have been used in studies of various pain populations (Arnold, Zlateva, Sadosky, Emir, & Whalen, 2011; Mohammad et al., 2014). Also, this measure has been recommended by the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) for use in clinical trials involving chronic pain (Dworkin et al., 2005). It takes less than one minute to complete.

3.3.2 ECG procedures

An ECG will be given to assess heart rate variability. In accordance with recommendations from the European Society of Cardiology and North American Society of Pacing and Electrophysiology Task Force ("Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology," 1996), the reading will occur for 5 minutes while the patient is lying down (for ease of electrode placement). We will obtain several measurements, including the standard deviation of the average NN (normal-to-normal) interval (SDANN) and the square root of the mean squared differences of successive NN intervals

(RMSSD). At baseline and follow-up visits, we will attempt to take measurements at approximately the same time of the day, since HRV can fluctuate throughout the day. Since the Wait-List group will essentially have two baseline assessments (one at enrollment and one before they start the ACT intervention), patients in this group will have three ECGs while the Immediate Intervention group will get a total of two ECGs. A standard "ECG Procedures" form will be used to capture any abnormalities in administration, such as if a patient coughs or talks during the administration. This form also will record whether the patient had any caffeine that day, and approximately how much, since caffeine can impact heart rate.

3.3.3 Word Reading test

The Word Reading subtest from the Wide Range Achievement Test 4 will be administered to patients in order to estimate their reading ability. This task is also a widely recognized proxy of cognitive functioning. This will allow us to control for this variable statistically, if there are any systematic differences related to how people with different reading skills (and proximal cognitive abilities) respond to the intervention, which is conceptually diverse and involves reading weekly emails. For this task, patients are asked to read a list of words aloud to the examiner. The Word Reading subtest takes about one to two minutes to complete.

3.4 STUDY CALENDAR

Procedure	**Screening**	**Baseline**	**Week 8**	**Week16**	**Week 32**	**Week 40**
History and Physical Exam	X					
Pain Interference Index	X					
Questionnaires*						
• ACT		X	X		X	
• WL		X	X	X		X
Word Reading						
• ACT		X				
• WL		X				
Electrocardiogram						
• ACT		X	X			
• WL		X	X	X		
Intervention						
• ACT		X				
• WL			X			
Adverse Events		X	X	X	X	X

*as listed in Section 3.3.1.

3.5 COMPENSATION

To thank participants for their time during participation, participants will receive $30 for each visit. Funds will be distributed in accordance with the Clinical Center's Research Volunteer system, such that participants can have the money directly deposited to a bank account or have a check mailed to them.

3.6 CRITERIA FOR REMOVAL FROM PROTOCOL

Participants will be removed from this study for any of the following:

- Screen failure
- Completion of protocol requirements
- Participant requests to be withdrawn from study
- Patient begins a new treatment that is likely to impact pain (e.g., MEK inhibitor)
- Patient reports a significant increase in pain that necessitates a new pain treatment or a medical procedure (i.e., surgery) that would notably impact pain levels. (These patients could re-enroll at a later date, if they again met criteria for this study and had not received the full in-person ACT intervention).
- Lost to follow up
- Investigator feels that it is in the best interest of the participant to withdraw from participation.

Note: all minors, who have signed the standard consent or assent, will be kept on study and followed until the age of 18 to allow consent.

3.6.1 Off-Study Procedure

Authorized staff will notify Central Registration Office (CRO) when a subject is taken off-study. A Participant Status Updates Form from the website (http://home.ccr.cancer.gov/intra/eligibility/welcome.htm) main page must be completed and sent via encrypted email to: NCI Central Registration Office ncicentralregistration-l@mail.nih.gov.

4 DATA COLLECTION AND EVALUATION

4.1 DATA COLLECTION

All questionnaires will be administered via computer or mobile tablet devices. The PI will be responsible for overseeing entry of data into an in-house password protected electronic system and ensuring data accuracy, consistency and timeliness. The principal investigator, associate investigators/research nurses and/or a contracted data manager will assist with the data management efforts. All data obtained during the conduct of the protocol will be kept in secure network drives or in approved alternative sites that comply with NIH security standards. Primary and final analyzed data will have identifiers so that research data can be attributed to an individual human subject participant.

Adverse events occurring as a result of treatment for the underlying condition or medical treatment for pain will NOT be recorded or reported on this study.

End of study procedures: Data will be stored according to HHS, FDA regulations, and NIH Intramural Records Retention Schedule as applicable.

Loss or destruction of data: Should we become aware that a major breach in our plan to protect subject confidentiality and trial data has occurred, the IRB will be notified.

5 SAFETY REPORTING REQUIREMENTS/DATA AND SAFETY MONITORING PLAN

5.1 DEFINITIONS

5.1.1 Adverse Event

An adverse event is defined as any reaction, side effect, or untoward event that occurs during the course of the clinical trial associated with the intervention, whether or not the event is considered related to the treatment or clinically significant.

For this study, AEs will primarily include events reported by the patient. Since this is a behavioral intervention and no drug therapy will be administered on this study, physical signs and symptoms as adverse events are not anticipated. A new illness, symptom, sign or clinically significant laboratory abnormality or worsening of a pre-existing condition or abnormality that occurs during the NIH visit which is not directly related to the participation in the baseline treatment sessions or completing the baseline questionnaires will not be reported on this study, but will be referred to the medical physician responsible for the participant's care. All AEs must be recorded on the AE case report form unless otherwise noted above in Section **4.1**.

5.1.2 Suspected adverse reaction

Suspected adverse reaction means any adverse event for which there is a reasonable possibility that study participation caused the adverse event. For the purposes of safety reporting, 'reasonable possibility' means there is evidence to suggest a causal relationship between study participation and the adverse event. A suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction, which means any adverse event caused by study participation.

5.1.3 Unexpected adverse reaction

An adverse event or suspected adverse reaction is considered "unexpected" if it is not listed in the protocol or is not listed at the specificity or severity that has been observed. "Unexpected", also refers to adverse events or suspected adverse reactions that are mentioned in the protocol or consent but not at the severity or frequency indicated.

5.1.4 Serious

An Unanticipated Problem or Protocol Deviation is serious if it meets the definition of a Serious Adverse Event or if it compromises the safety, welfare or rights of subjects or others.

5.1.5 Serious Adverse Event

An adverse event or suspected adverse reaction is considered serious if in the view of the investigator or the sponsor, it results in any of the following:

- Death,
- A life-threatening adverse experience
- Inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- A congenital anomaly/birth defect.
- Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse drug experience when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

5.1.6 Disability

A substantial disruption of a person's ability to conduct normal life functions.

5.1.7 Protocol Deviation (NIH Definition)

Any change, divergence, or departure from the IRB-approved research protocol.

5.1.8 Non-compliance (NIH Definition)

The failure to comply with applicable NIH Human Research Protections Program (HRPP) policies, IRB requirements, or regulatory requirements for the protection of human research subjects.

5.1.9 Unanticipated Problem

Any incident, experience, or outcome that:

- Is unexpected in terms of nature, severity, or frequency in relation to
  (a) the research risks that are described in the IRB-approved research protocol and informed consent document; Investigator's Brochure or other study documents, and
  (b) the characteristics of the subject population being studied; **AND**
- Is related or possibly related to participation in the research; **AND**
- Suggests that the research places subjects or others at a g*reater risk of harm* (including physical, psychological, economic, or social harm) than was previously known or recognized.

5.2 NIH INTRAMURAL IRB AND CLINICAL DIRECTOR REPORTING

5.2.1 NIH Intramural IRB and NCI CD Expedited Reporting of Adverse Events, Unanticipated Problems, and Deaths

The Protocol PI will report in the NIH Problem Form to the NIH Intramural IRB and NCI Clinical Director:

- All deaths, except deaths due to progressive disease
- All Protocol Deviations
- All Unanticipated Problems
- All non-compliance

Reports must be received within 7 days of PI awareness via iRIS.

5.2.2 NIH Intramural IRB Requirements for PI Reporting of Adverse Events at Continuing Review

The protocol PI will report to the NIH Intramural IRB:

1. A summary of all protocol deviations in a tabular format to include the date the deviation occurred, a brief description of the deviation and any corrective action.
2. A summary of any instances of non-compliance
3. A tabular summary of the following adverse events:
    - All Grade 2 **unexpected** events that are possibly, probably or definitely related to the research;
    - All Grade 3 and 4 events that are possibly, probably or definitely related to the research;
    - All Grade 5 events regardless of attribution;
    - All Serious Events regardless of attribution.

   NOTE: Grade 1 events are not required to be reported.

5.3 DATA AND SAFETY MONITORING PLAN

5.3.1 Principal Investigator/Research Team

The clinical research team will meet on a regular basis to ensure that treatment implementation and follow up data collection are organized and completed in a timely fashion. The principal investigator or AI will review all data within one week of submission. Adverse events will be reported as required above. Any safety concerns, new information that might affect either the ethical and or scientific conduct of the trial, or protocol deviations will be immediately reported to the NIH Intramural IRB using iRIS.

The principal investigator will review adverse event and response data on each patient to ensure safety and data accuracy. The principal investigator will personally conduct or supervise the investigation and provide appropriate delegation of responsibilities to other members of the research staff.

6 STATISTICAL SECTION

6.1 PRIMARY AND SECONDARY OUTCOMES

The primary objective of the trial is to compare pain interference mean score changes from baseline to 8 weeks between the ACT intervention group and the WL group. In the pilot study conducted by our group, mean scores on PII self-report went from 2.1 (1.0) to 1.5 (1.1), with paired differences having a mean change of -0.68 and SD=1.3. Based on this preliminary estimated change for the ACT group, and an assumption of no change in the WL group and a corresponding, reduced SD = 0.8, forty-one patients will be needed per group to have 80% power to detect a difference in change score between the two arms of -0.68, using a t-test with significance level of .05 (two-sided). Secondary analyses will be performed to compare between-group changes from baseline to 8 weeks and from baseline to 32 weeks on the following endpoints: disease-related quality of life, pain severity, pain-related anxiety, and depression. Given the wide age range of the study, we will stratify analyses by age (16 – 24 years; 25 – 59 years). Descriptive statistics will be computed on the primary and secondary outcome measures (means, standard deviations, etc.). If there are significant differences between the groups at baseline (for example, with respect to gender or number of patients on pain medication), analysis of covariance (ANCOVA) may be used to control for these differences statistically during follow-up analyses (treating baseline as a covariate). We also will assess for differences between the group randomized to ACT and the WL group on primary and secondary outcomes, particularly comparing primary results from 0 to 8 weeks for ACT vs. 8 to 16 weeks for WL (receiving ACT starting at 8 weeks); if the results are similar (for example, $p>0.30$ approximately), we will combine these groups to report the overall effect of ACT for 8 weeks, and also examine changes from baseline to 8 weeks and 8 to 16 weeks using an appropriate statistical test. Finally, based on a priori hypotheses and prior literature, we will test for indirect effects of acceptance and psychological flexibility with simple mediation model analyses. We will generate 5,000 bootstrapped samples using Preacher and Hayes' (Preacher & Hayes, 2004) INDIRECT macro. Post-treatment scores will be used for these analyses. Additionally, we will examine whether a previous cognitive diagnosis (ADHD or learning disability), reading ability, disease characteristics (stable vs. progressive disease, location of plexiform neurofibroma), or recent life events, relate to changes over time in the primary outcome with an ANOVA, and if so we may control for these variables in other analyses with an ANCOVA. Finally, we will compare the psychometric properties of the PII and PROMIS Pain Interference Scale by examining internal consistency in the patient sample (computed by Pearson correlations) and the response to change (as described in the primary objective analysis above). Data will be entered into a secure database, then analyzed using SAS statistical software.

6.2 SUBJECT ACCRUAL

We will attempt to enroll up to 41 patients per group. Patients who complete the WL arm of the study will cross-over to the ACT arm. To provide for patients who enroll but then drop out before completing all follow-up measures, we will attempt to enroll up to 90 patients total. As of January 2015, approximately 70 of the patients enrolled on the NF1 Natural History study (08-C-0079) are within the eligible age range of the study, and are not on a MEK inhibitor trial (or planning to start one in the next six months). In addition, about 300 individuals are signed up on the CTF registry and are within the study's age range and have a PN. We will email these individuals as another recruitment source (see Appendices S & T for emails). Additionally, we will send email fliers to other NF clinics in the U.S. that see patients within this study's age range (e.g., Johns Hopkins, University of Chicago, Massachusetts General Hospital, etc.). The flier is in **Appendix W**. If 5 – 6 patients per month are entered onto this intervention study, data collection could be completed within 30 months. Given that external funding will provide a full-term postdoctoral fellow who will help with scheduling and will conduct the majority of the ACT treatment sessions, this is presumed to be a reasonable goal.

7 HUMAN SUBJECTS PROTECTIONS

7.1 RATIONALE FOR SUBJECT SELECTION

Neurofibromatosis type 1 is a genetic disorder with a worldwide incidence of 1:3500 individuals. No groups, in regards to gender, race or ethnicity, are being excluded from participation in the trial. Because the research on the effectiveness of ACT with younger adolescents is still emerging, children 15 and younger will be excluded from the present study.

7.2 PARTICIPATION OF CHILDREN

Children 16-17 years of age will be entered onto this research trial. Children will be evaluated by clinicians trained in pediatrics, and will be cared for in the pediatric clinic or outpatient setting. Some of the participants will be co-enrolled on Dr. Brigitte Widemann's NCI protocol 08-C-0079 (Natural History Study and Longitudinal Assessment of Children, Adolescents, and Adults with Neurofibromatosis Type 1), where the physical needs of participants will be addressed. If patients require hospital admission, they will be cared for on the pediatric unit of the CRC by the POB staff or on the adult unit of the CRC, depending on age.

7.3 PARTICIPATION OF SUBJECTS UNABLE TO GIVE CONSENT

Subjects unable to give consent are excluded from enrolling in the protocol. Should the subject become decisionally impaired during participation he/she will be removed from study as they will no longer be capable of completing the research interventions.

7.4 EVALUATION OF BENEFITS AND RISKS/DISCOMFORTS.

As this is a behavioral intervention study, no medical treatments will be administered and therefore the risks are considered minimal. The completion of questionnaires requires a maximum of 35 minutes at baseline and follow-up time points. Although we do not anticipate this, one potential risk of participation is significantly increased levels of anxiety related to the sessions, such as discussing the impact of pain on quality of life and the time involved in completing exercises at home. The study's PI (Dr. Martin Peron) and the other trainers will be closely monitoring patients for any such distress. They are prepared to address any signs or symptoms of anxiety or emotional distress that occur throughout the sessions. Also, if patients endorse a significant level of depression on the CES-D, defined as a raw score of 27 or higher (Geisser, Roth, & Robinson, 1997), Dr. Martin Peron or another trainer under Dr. Martin Peron's supervision will be available to respond (this form will be checked within 24 hours of completion and before the patient leaves the NIH). Responses could include discussing these concerns with the participant, referral for a psychiatry consult while at the NIH, and/or providing referrals for therapeutic services in the participant's local area beyond the scope of the intervention. Any services provided at the NIH in response to an urgent psychological problem that occurs during the workshop will be at no cost to the participant. While this is not anticipated to be necessary, if it is judged to be in the best interest of the participant to stop the study sessions prematurely, this will be done. Another small risk is involved with electrocardiogram, in that the person may develop a mild rash where the electrodes were attached. This is rare, and the rash often goes away without treatment.

The research on ACT to date indicates that it is at least as helpful as standard care and other methodologies (e.g., traditional cognitive-behavioral therapy, relaxation training) for individuals with various types of pain, and more effective than treatment as usual or inactive control groups. Thus, there is the potential for direct benefit to participants.

For participants who are 16-17, this research does not involve greater than minimal risk, and participants in this age group will be provided with the opportunity to assent to participate. Hence this study meets the requirements of 45 CFR 46.404 in that it does not involve greater than minimal risk, but there may also be the potential for direct benefit from participation.

7.5 CONSENT AND ASSENT PROCESS AND DOCUMENTATION

The questionnaires and training sessions involved in this study and the attendant risks, discomforts and benefits of these processes, will be carefully explained to the patient and the patient's parents or guardian if he/she is a minor. All family members who are present will be given the opportunity to ask questions. Patients (and parents in the case of minors) will be given the opportunity to discuss their decision privately for as long as they request, either in the clinic room or in a location of their choice. A signed informed consent document will be obtained prior to entry onto the study and completion of baseline questionnaires. Written consent or assent for children 16-17 years of age for participation in this study will be obtained by the principal investigator or an associate investigator.

For adolescent participants (ages 16-17 years), the investigators are requesting a waiver from the IRB to allow only one parent to sign the informed consent for protocol entry. Because many patients must travel to the NIH from long distances at substantial expense, requiring both parents to be present for the consent process could be a financial hardship for many families. The PI or an associate investigator will obtain consent in all cases. When guardianship status of the child is uncertain, documentation of custody status must be obtained.

In situations where there is joint custody of a child, both parents must sign consent. If only one parent can be present at NIH, the other parent's consent can be obtained by telephone via the procedure described in section **7.5.3**.

Where deemed appropriate by the clinician and the adolescent's parent(s) or guardian, the adolescent will also be included in all discussions about the trial and age-appropriate language will be used to describe the procedures and tests involved in this study, along with the risks, discomforts and benefits of participation. Adolescents under the age of 18, but who are age ≥16 or older will be asked to sign an age appropriate assent form. The consent/assent process will be documented in the adolescent's medical record, including the assessment of the adolescent's ability to provide assent (verbal versus written) as applicable.

7.5.1 Request for waiver of consent for screening evaluation

Although consent will be obtained prior to enrollment on this study, a waiver is requested for obtaining informed consent to send recruitment e-mails and to conduct initial screening questions over the phone. According to OHRP, "In order to permit investigators to obtain and record identifiable private information for the purposes of identifying potential subjects, OHRP expects that IRBs routinely will waive the requirement for informed consent for such activities. In assessing the level of risk to determine whether a waiver of informed consent or parental permission is permissible for the identification of potential subjects, the IRB need only consider the risk of investigators accessing the subjects' identifiable private information, not the risks of the research in toto. (From Frequently asked questions from OHRP: http://answers.hhs.gov/ohrp/categories/1566).

7.5.2 Consent for minors when they reach the age of majority

When a pediatric subject reaches age 18, continued participation (including ongoing interactions with the subject or continued analysis of identifiable data) will require consenting of the now adult with the standard protocol consent document to ensure legally effective informed consent has been obtained. Given the length of time that has transpired for some of the subjects since their last visit for this study, we request waiver of informed consent for those individuals who have completed their participation in the research study.

Requirements for Waiver of Consent consistent with 45 CFR 46.116 (d):

(1) The research involves no more than minimal risk to the subjects.
    a. Analysis of samples and data from this study involves no additional risks to subjects.
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects.
    a. Retention of these samples or data does not affect the welfare of subjects.
(3) The research could not practicably be carried out without the waiver or alteration.
    a. Considering the length of time between a minor's enrollment and their age of majority, it is possible that more than a few subjects may be lost to follow

up. A significant reduction in the number of samples analyzed could impact the quality of the research.

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

   a. We only plan to request a waiver of consent for those subjects who have been lost to follow-up or who, prior to the approval of Amendment D, have been taken off study prior to reaching the age of majority.

7.5.3 Telephone consent

The informed consent document will be sent to the subject. An explanation of the study will be provided over the telephone after the subject has had the opportunity to read the consent form. The subject will sign and date the informed consent.

The original informed consent document will be sent back to the consenting investigator who will sign and date the consent form with the date the consent was obtained via telephone.

A fully executed copy will be returned via mail for the subject's records.

The informed consent process will be documented on a progress note by the consenting investigator.

7.5.4 Telephone assent

The informed consent and assent documents will be sent to the parents/guardian and child. An explanation of the study will be provided over the telephone after the parents/guardian and child have had the opportunity to read the documents. Age-appropriate language will be used to discuss the study with the child. The parents/guardian will sign and date the informed consent, including the line for verbal assent of a child if appropriate. If an assent form is used (see above for when an assent form will be used), the child will sign and date that form.

The original signed informed consent and assent documents will be sent back to the consenting investigator who will sign and date the consent form with the date the consent was obtained via telephone.

A fully executed copy will be returned via mail to the subject.

The informed consent and assent process will be documented on a progress note by the consenting investigator.

8 REFERENCES

Amtmann, D., Cook, K. F., Jensen, M. P., Chen, W. H., Choi, S., Revicki, D., . . . Lai, J. S. (2010). Development of a PROMIS item bank to measure pain interference. *Pain, 150*(1), 173-182. doi: 10.1016/j.pain.2010.04.025

Appelhans, B. M., & Luecken, L. J. (2008). Heart rate variability and pain: associations of two interrelated homeostatic processes. *Biol Psychol, 77*(2), 174-182. doi: 10.1016/j.biopsycho.2007.10.004

Arnold, L. M., Zlateva, G., Sadosky, A., Emir, B., & Whalen, E. (2011). Correlations between fibromyalgia symptom and function domains and patient global impression of change: a pooled analysis of three randomized, placebo-controlled trials of pregabalin. *Pain Med, 12*(2), 260-267. doi: 10.1111/j.1526-4637.2010.01047.x

Bach, P., & Hayes, S. C. (2002). The use of acceptance and commitment therapy to prevent the rehospitalization of psychotic patients: a randomized controlled trial. *Journal of Consulting and Clinical Psychology, 70*(5), 1129-1139.

Baranoff, J., Hanrahan, S. J., Kapur, D., & Connor, J. P. (2013). Acceptance as a process variable in relation to catastrophizing in multidisciplinary pain treatment. *European Journal of Pain, 17*(1), 101-110. doi: 10.1002/j.1532-2149.2012.00165.x

Benarroch, E. E. (2006). Pain-autonomic interactions. *Neurol Sci, 27 Suppl 2*, S130-133. doi: 10.1007/s10072-006-0587-x

Berry, M. E., Chapple, I. T., Ginsberg, J. P., Gleichauf, K. J., Meyer, J. A., & Nagpal, M. L. (2014). Non-pharmacological Intervention for Chronic Pain in Veterans: A Pilot Study of Heart Rate Variability Biofeedback. *Glob Adv Health Med, 3*(2), 28-33. doi: 10.7453/gahmj.2013.075

Brems, H., Park, C., Maertens, O., Pemov, A., Messiaen, L., Upadhyaya, M., . . . Stewart, D. R. (2009). Glomus tumors in neurofibromatosis type 1: genetic, functional, and clinical evidence of a novel association. *Cancer Research, 69*(18), 7393-7401. doi: 0008-5472.CAN-09-1752 [pii] 10.1158/0008-5472.CAN-09-1752

Buhrman, M., Skoglund, A., Husell, J., Bergstrom, K., Gordh, T., Hursti, T., . . . Andersson, G. (2013). Guided internet-delivered acceptance and commitment therapy for chronic pain patients: a randomized controlled trial. *Behav Res Ther, 51*(6), 307-315. doi: 10.1016/j.brat.2013.02.010

Burns, K.M., Wolters, P. L., Martin, S., Baldwin, A., Dombi, E., Kurwa, A., . . . Widemann, B. (2011a). *Parent and self reports of pain in children and adolescents with neurofibromatosis-type 1 (NF1) and plexiform neurofibromas: relation to quality of life, social-emotional functioning, and physical manifestations.* Paper presented at the National Conference in Pediatric Psychology, San Antonio, TX.

Burns, K.M., Wolters, P., Martin, S., Baldwin, A., Dombi, E., Kurwa, A., . . . Widemann, B. (2011b). *Parent and self reports of pain in children and adolescents with neurofibromatosis type 1 (NF1) and plexiform neurofibromas: relation to quality of life, social-emotional functioning, and physical manifestations.* Paper presented at the National Conference in Pediatric Psychology, San Antonio, TX.

Butryn, M. L., Forman, E., Hoffman, K., Shaw, J., & Juarascio, A. (2011). A pilot study of acceptance and commitment therapy for promotion of physical activity. *Journal of Physical Activity & Health, 8*(4), 516-522.

Chiesa, A., & Serretti, A. (2010). A systematic review of neurobiological and clinical features of mindfulness meditations. *Psychological Medicine, 40*(8), 1239-1252. doi: S0033291709991747 [pii] 10.1017/S0033291709991747

Chiesa, A., & Serretti, A. (2011). Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. *Psychiatry Research, 187*(3), 441-453. doi: S0165-1781(10)00519-6 [pii] 10.1016/j.psychres.2010.08.011

Dahl, J., Wilson, K. G., Luciano, C, & Hayes, S. C. (2005). *Acceptance and Commitment Therapy for Chronic Pain*. Reno, NV: Context Press.

Dahl, J., Wilson, K. G., & Nilsson, A. (2004). Acceptance and commitment therapy and the treatment of persons at risk for long-term disability resulting from stress and pain symptoms: A preliminary randomized trial. *Behavior Therapy, 35*(4), 785-801.

Davies, C. D., Niles, A. N., Pittig, A., Arch, J. J., & Craske, M. G. (2015). Physiological and behavioral indices of emotion dysregulation as predictors of outcome from cognitive behavioral therapy and acceptance and commitment therapy for anxiety. *J Behav Ther Exp Psychiatry, 46*, 35-43. doi: 10.1016/j.jbtep.2014.08.002

DiMario, F.J., & Langshur, S. (2000). Headaches in patients with neurofibromatosis-1. *Journal of Child Neurology, 15*, 235-238.

Dombi, E., Solomon, J., Gillespie, A.J., Fox, E., Balis, F.M., Patronas, N., . . . Widemann, B.C. (2007). NF1 plexiform neurofibroma growth rate by volumetric MRI: Relation to age and body weight. *Neurology, 68*, 643-647.

Dworkin, R. H., Turk, D. C., Farrar, J. T., Haythornthwaite, J. A., Jensen, M. P., Katz, N. P., . . . Witter, J. (2005). Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain, 113*(1-2), 9-19. doi: 10.1016/j.pain.2004.09.012

Elliott-Desorbo, D. K., Martin, S., & Wolters, P. L. (2009). Stressful Life Events and Their Relationship to Psychological and Medical Functioning in Children and Adolescents With HIV Infection. *Journal of Acquired Immune Deficiency Syndromes*.

Espie, C. A., Kyle, S. D., Williams, C., Ong, J. C., Douglas, N. J., Hames, P., & Brown, J. S. (2012). A randomized, placebo-controlled trial of online cognitive behavioral therapy for chronic insomnia disorder delivered via an automated media-rich web application. *Sleep, 35*(6), 769-781. doi: 10.5665/sleep.1872

Evans, S., Seidman, L. C., Tsao, J. C., Lung, K. C., Zeltzer, L. K., & Naliboff, B. D. (2013). Heart rate variability as a biomarker for autonomic nervous system response differences between children with chronic pain and healthy control children. *J Pain Res, 6*, 449-457. doi: 10.2147/jpr.s43849

Forman, E. M., Herbert, J. D., Moitra, E., Yeomans, P. D., & Geller, P. A. (2007). A randomized controlled effectiveness trial of acceptance and commitment therapy and cognitive therapy for anxiety and depression. *Behavior Modification, 31*(6), 772-799. doi: 31/6/772 [pii] 10.1177/0145445507302202

Freeman, K. A., Duke, D. C., & Harris, M. A. (2013). Behavioral health care for adolescents with poorly controlled diabetes via Skype: does working alliance remain intact? *J Diabetes Sci Technol, 7*(3), 727-735.

Friedrich, R. E., Schmelzle, R., Hartmann, M., Funsterer, C., & Mautner, V. F. (2005). Resection of small plexiform neurofibromas in neurofibromatosis type 1 children. *World Journal of Surgical Oncology, 3*(1), 6. doi: 1477-7819-3-6 [pii] 10.1186/1477-7819-3-6

Garrison, C. Z., Addy, C. L., Jackson, K. L., McKeown, R. E., & Waller, J. L. (1991). The CES-D as a screen for depression and other psychiatric disorders in adolescents. *Journal of the American Academic of Child and Adolescent Psychiatry, 30*(4), 636-641. doi: S0890-8567(09)64332-X [pii] 10.1097/00004583-199107000-00017

Geisser, M. E., Roth, R. S., & Robinson, M. E. (1997). Assessing depression among persons with chronic pain using the Center for Epidemiological Studies and the Beck Depression Inventory: a comparative analysis. *The Clinical Journal of Pain, 13*, 163-170.

Georgescu, E. F., Stanescu, L., Georgescu, A. C., Dumitrescu, D., Foarfa, C., & Calin, G. (2007). Bone abnormalities occurring in the follow-up of the patients with neurofibromatosis type 1. *Romainian Journal of Morphology and Embryology, 48*(3), 249-256. doi: 480307249256 [pii]

Gutmann, D. H., Aylsworth, A., Carey, J. C., Korf, B., Marks, J., Pyeritz, R. E., . . . Viskochil, D. (1997). The diagnostic evaluation and multidisciplinary management of neurofibromatosis 1 and neurofibromatosis 2. *JAMA-Journal of the American Medical Association, 278*(1), 51-57.

Hann, D., Winter, K., & Jacobsen, P. (1999). Measurement of depressive symptoms in cancer patients: evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *Journal of Psychosomatic Research, 46*(5), 437-443. doi: S0022399999000045 [pii]

Hayes, S. C., & Strosahl, K. D. (2004). *A practical guide to Acceptance and Commitment Therapy*. New York: Springer-Verlag.

Hayes, S. C., Strosahl, K.D., & Wilson, K. G. (1999). *Acceptance and Commitment Therapy: An Experiential Approach to Behavior Change*. New York, NY: The Guilford Press.

Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). *Eur Heart J, 17*(3), 354-381.

Hernandez-Lopez, M., Luciano, M. C., Bricker, J. B., Roales-Nieto, J. G., & Montesinos, F. (2009). Acceptance and commitment therapy for smoking cessation: a preliminary study of its effectiveness in comparison with cognitive behavioral therapy. *Psychology of Addictive Behaviors, 23*(4), 723-730. doi: 2009-24023-020 [pii] 10.1037/a0017632

Heuschkel, R., Kim, S., Korf, B., Schneider, G., & Bousvaros, A. (2001). Abdominal migraine in children with neurofibromatosis type 1: a case series and review of gastrointestinal involvement in NF1. *Journal of Pediatric Gastroenterology and Nutrition, 33*(2), 149-154.

Hofmann, S. G., Sawyer, A. T., Witt, A. A., & Oh, D. (2010). The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *Journal of Consulting and Clinical Psychology, 78*(2), 169-183. doi: 2010-05835-004 [pii] 10.1037/a0018555

Holzel, B. K., Carmody, J., Vangel, M., Congleton, C., Yerramsetti, S. M., Gard, T., & Lazar, S. W. (2011). Mindfulness practice leads to increases in regional brain gray matter density. *Psychiatry Research, 191*(1), 36-43. doi: S0925-4927(10)00288-X [pii] 10.1016/j.pscychresns.2010.08.006

Howorka, K., Pumprla, J., Tamm, J., Schabmann, A., Klomfar, S., Kostineak, E., . . . Sovova, E. (2013). Effects of guided breathing on blood pressure and heart rate variability in hypertensive diabetic patients. *Auton Neurosci, 179*(1-2), 131-137. doi: 10.1016/j.autneu.2013.08.065

Huggins, J. L., Bonn-Miller, M. O., Oser, M. L., Sorrell, J. T., & Trafton, J. A. (2012). Pain anxiety, acceptance, and outcomes among individuals with HIV and chronic pain: a preliminary investigation. *Behav Res Ther, 50*(1), 72-78. doi: 10.1016/j.brat.2011.10.008

Hyman, S. L., Shores, A. E., & North, K. N. (2006). Learning disabilities in children with neurofibromatosis type 1: subtypes, cognitive profile, and attention-deficit-hyperactivity disorder.

Developmental Medicine and Child Neurology, 48(12), 973-977. doi: 10.1017/S0012162206002131

Jett, K., & Friedman, J. M. (2010). Clinical and genetic aspects of neurofibromatosis 1. [Review]. *Genetics in Medicine, 12*(1), 1-11. doi: 10.1097/GIM.0b013e3181bf15e3

Jiang, W., Ladd, S., Martsberger, C., Feinglos, M., Spratt, S. E., Kuchibhatla, M., . . . Krishnan, R. (2011). Effects of pregabalin on heart rate variability in patients with painful diabetic neuropathy. *J Clin Psychopharmacol, 31*(2), 207-213. doi: 10.1097/JCP.0b013e31820f4f57

Kabat-Zinn, J. (1990). *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain, and Illness*. New York, NY: Bantam Dell.

Kabat-Zinn, J, Lipworth, L, Burney, R, & Sellers, W. (1986). Four-year-follow-up of a meditation-based program for the self-regulation of chronic pain: Treatment outcomes and compliance. *Clinical Journal of Pain, 2*, 159-173.

Kim, A., Gillespie, A., Dombi, E., Goodwin, A., Goodspeed, W., Fox, E., . . . Widemann, B. C. (2009). Characteristics of children enrolled in treatment trials for NF1-related plexiform neurofibromas. *Neurology, 73*(16), 1273-1279. doi: 10.1212/WNL.0b013e3181bd1326

Kirkpatrick, T., Manoukian, L., Dear, B. F., Johnston, L., & Titov, N. (2013). A feasibility open trial of internet-delivered cognitive-behavioural therapy (iCBT) among consumers of a non-governmental mental health organisation with anxiety. *PeerJ, 1*, e210. doi: 10.7717/peerj.210

Klaren, R. E., Hubbard, E. A., & Motl, R. W. (2014). Efficacy of a behavioral intervention for reducing sedentary behavior in persons with multiple sclerosis: a pilot examination. *Am J Prev Med, 47*(5), 613-616. doi: 10.1016/j.amepre.2014.05.036

Koenig, J., Jarczok, M. N., Ellis, R. J., Hillecke, T. K., & Thayer, J. F. (2013). Heart rate variability and experimentally induced pain in healthy adults: A systematic review. *European Journal of Pain*. doi: 10.1002/j.1532-2149.2013.00379.x

Kristiansen, J., Ektor-Andersen, J., Bondesson, E., Orbaek, P., Persson, R., Garde, A. H., & Hansen, A. M. (2011). Low heart rate variability is associated with extended pain-related sick leave among employed care-seekers. *J Rehabil Med, 43*(11), 976-982. doi: 10.2340/16501977-0882

Leykin, Y., Thekdi, S. M., Shumay, D. M., Munoz, R. F., Riba, M., & Dunn, L. B. (2012). Internet interventions for improving psychological well-being in psycho-oncology: review and recommendations. *Psychooncology, 21*(9), 1016-1025. doi: 10.1002/pon.1993

Martin, S., Gillespie, A., Wolters, P. L., & Widemann, B. C. (2011). Experiences of families with a child, adolescent, or young adult with neurofibromatosis type 1 and plexiform neurofibroma evaluated for clinical trials participation at the National Cancer Institute. [Article]. *Contemporary Clinical Trials, 32*(1), 10-15. doi: 10.1016/j.cct.2010.10.004

Martin, S., Nelson Schmitt, S., Wolters, P. L., Abel, B., Toledo-Tamula, M. A., Baldwin, A., . . . Widemann, B. (2014). Development and Validation of the English Pain Interference Index and Pain Interference Index-Parent Report. *Pain Med*. doi: 10.1111/pme.12620

Martin, S., Wolters, P., Toledo-Tamula, M. A., Nelson Schmitt, S., Baldwin, A., Starosta, A., . . . Widemann, B. (manuscript accepted). Acceptance and commitment therapy in youth with Neurofibromatosis Type 1 (NF1) and chronic pain and their parents: a pilot study. *Pain Practice*.

Masuda, A., Cohen, L. L., Wicksell, R. K., Kemani, M. K., & Johnson, A. (2011). A Case Study: Acceptance and Commitment Therapy for Pediatric Sickle Cell Disease. [Article]. *Journal of Pediatric Psychology, 36*(4), 398-408. doi: 10.1093/jpepsy/jsq118

McCracken, L. M., & Dhingra, L. (2002). A short version of the Pain Anxiety Symptoms Scale (PASS-20): preliminary development and validity. [Validation Studies]. *Pain Res Manag, 7*(1), 45-50.

McCracken, L. M., MacKichan, F., & Eccleston, C. (2007). Contextual cognitive-behavioral therapy for severely disabled chronic pain sufferers: effectiveness and clinically significant change. *European Journal of Pain, 11*(3), 314-322. doi: 10.1016/j.ejpain.2006.05.004

McCracken, L. M., Sato, A., & Taylor, G. J. (2013). A trial of a brief group-based form of acceptance and commitment therapy (ACT) for chronic pain in general practice: pilot outcome and process results. *The Journal of Pain, 14*(11), 1398-1406. doi: 10.1016/j.jpain.2013.06.011

McCracken, L. M., Vowles, K. E., & Eccleston, C. (2004). Acceptance of chronic pain: component analysis and a revised assessment method. *Pain, 107*(1-2), 159-166. doi: S0304395903004299 [pii]

McCracken, L., & Zhao-O'Brien, J. (2010). General psychological acceptance and chronic pain: There is more to accept than the pain itself. *European Journal of Pain, 14*, 170-175.

Merkes, M. (2010). Mindfulness-based stress reduction for people with chronic diseases. *Australian Journal of Primary Health, 16*(3), 200-210. doi: PY09063 [pii] 10.1071/PY09063

Mohammad, S., Di Lorenzo, C., Youssef, N. N., Miranda, A., Nurko, S., Hyman, P., & Saps, M. (2014). Assessment of abdominal pain through global outcomes and recent FDA recommendations in children: are we ready for change? *J Pediatr Gastroenterol Nutr, 58*(1), 46-50. doi: 10.1097/MPG.0b013e3182a20764

Nutakki, K., Hingtgen, C. M., Monahan, P., Varni, J. W., & Swigonski, N. L. (2013). Development of the adult PedsQL neurofibromatosis type 1 module: initial feasibility, reliability and validity. *Health Qual Life Outcomes, 11*, 21. doi: 10.1186/1477-7525-11-21

Orme, J. G., Reis, J., & Herz, E. J. (1986). Factorial and discriminant validity of the Center for Epidemiological Studies Depression (CES-D) scale. *Journal of Clinical Psychology, 42*(1), 28-33.

Page, P. Z., Page, G. P., Ecosse, E., Korf, B. R., Leplege, A., & Wolkenstein, P. (2006). Impact of neurofibromatosis 1 on Quality of Life: A cross-sectional study of 176 American cases. *American Journal of Medical Genetics Part A, 140A*(18), 1893-1898.

Pearson, A., Follette, V., & Hayes, S. C. (2011). A pilot study of acceptance and commitment therapy as a workshop intervention for body dissatisfaction and disordered eating attitudes. *Cognitive and Behavioral Practice*.

Piet, J., & Hougaard, E. (2011). The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis. *Clinical Psychology Review, 31*(6), 1032-1040. doi: S0272-7358(11)00097-3 [pii] 10.1016/j.cpr.2011.05.002

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav Res Methods Instrum Comput, 36*(4), 717-731.

Radloff, L. S. (1977). The CES-D scale: a self-report depression scale for research in the general population. *Applied Psychological Measurement, 1*, 385-401.

Rainsford, K. D. (1999). Profile and mechanisms of gastrointestinal and other side effects of nonsteroidal anti-inflammatory drugs (NSAIDs). *American Journal of Medicine, 107*(6A), 27S-35S; discussion 35S-36S.

Reynard, A., Gevirtz, R., Berlow, R., Brown, M., & Boutelle, K. (2011). Heart rate variability as a marker of self-regulation. *Appl Psychophysiol Biofeedback, 36*(3), 209-215. doi: 10.1007/s10484-011-9162-1

Rieley, M. B., Stevenson, D. A., Viskochil, D. H., Tinkle, B. T., Martin, L. J., & Schorry, E. K. (2011). Variable expression of neurofibromatosis 1 in monozygotic twins. *American Journal of Medical Genetics Part A, 155A*(3), 478-485. doi: 10.1002/ajmg.a.33851

Robertson, B. (2011). The Adaptation and Application of Mindfulness-based Psychotherapeutic Practices for Individuals with Intellectual Disabiltiies. In R. Fletcher (Ed.), *Psychotherapy for Individuals with Intellectual Disability* (pp. 91-106): National Association for the Dually Diagnosed.

Rodriguez, R. F., Castillo, J. M., Castillo, M. P., Montoya, O., Daza, P., Rodriguez, M. F., . . . Angel, A. M. (2008). Hydrocodone/acetaminophen and tramadol chlorhydrate combination tablets for the management of chronic cancer pain: A double-blind comparative trial. [Article]. *Clinical Journal of Pain, 24*(1), 1-4.

Roelofs, J., McCracken, L., Peters, M. L., Crombez, G., van Breukelen, G., & Vlaeyen, J. W. (2004). Psychometric evaluation of the Pain Anxiety Symptoms Scale (PASS) in chronic pain patients. [Validation Studies]. *J Behav Med, 27*(2), 167-183.

Segerstrom, S. C., & Nes, L. S. (2007). Heart rate variability reflects self-regulatory strength, effort, and fatigue. *Psychol Sci, 18*(3), 275-281. doi: 10.1111/j.1467-9280.2007.01888.x

Stein, C., Dal Lago, P., Ferreira, J. B., Casali, K. R., & Plentz, R. D. (2011). Transcutaneous electrical nerve stimulation at different frequencies on heart rate variability in healthy subjects. *Auton Neurosci, 165*(2), 205-208. doi: 10.1016/j.autneu.2011.07.003

Swann, A. C. (2001). Major system toxicities and side effects of anticonvulsants. *Journal of Clinical Psychiatry, 62 Suppl 14*, 16-21.

Swendeman, D., Comulada, W. S., Ramanathan, N., Lazar, M., & Estrin, D. (2014). Reliability and Validity of Daily Self-Monitoring by Smartphone Application for Health-Related Quality-of-Life, Antiretroviral Adherence, Substance Use, and Sexual Behaviors Among People Living with HIV. *AIDS Behav*. doi: 10.1007/s10461-014-0923-8

Teasdale, J. D., Segal, Z. V., Williams, J. M., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology, 68*(4), 615-623.

Terkelsen, A. J., Molgaard, H., Hansen, J., Finnerup, N. B., Kroner, K., & Jensen, T. S. (2012). Heart rate variability in complex regional pain syndrome during rest and mental and orthostatic stress. *Anesthesiology, 116*(1), 133-146. doi: 10.1097/ALN.0b013e31823bbfb0

Thorsell, J., Finnes, A., Dahl, J., Lundgren, T., Gybrant, M., Gordh, T., & Buhrman, M. (2011). A Comparative Study of 2 Manual-based Self-Help Interventions, Acceptance and Commitment Therapy and Applied Relaxation, for Persons With Chronic Pain. *Clinical Journal of Pain*. doi: 10.1097/AJP.0b013e318219a933

Tonsgard, J.H. (2006). Clinical manifestations and management of neurofibromatosis type 1. *Seminars in Pediatric Neurology, 13*, 2-7.

Trompetter, H.R., Bohlmeijer, E.T., van Baalen, B., Kleen, M., Koke, A., Reneman, M., & Schreurs, K.M.G. (2014). The Psychological Inflexibility in Pain Scale (PIPS): Exploration of psychometric properties in a heterogeneous chronic pain sample. *European Journal of Psychological Assessment, 30*(4), 289-295.

Tucker, T., Friedman, J. M., Friedrich, R. E., Wenzel, R., Funsterer, C., & Mautner, V. F. (2009). Longitudinal study of neurofibromatosis 1 associated plexiform neurofibromas. [Article]. *Journal of Medical Genetics, 46*(2), 81-85. doi: 10.1136/jmg.2008.061051

Turk, D. C., & Okifuji, A. (1994). Detecting depression in chronic pain patients: adequacy of self-reports. *Behav Res Ther, 32*(1), 9-16.

Twohig, M. P., Hayes, S. C., & Masuda, A. (2006). Increasing willingness to experience obsessions: acceptance and commitment therapy as a treatment for obsessive-compulsive disorder. *Behavior Therapy, 37*(1), 3-13. doi: S0005-7894(06)00003-7 [pii] 10.1016/j.beth.2005.02.001

Varni, J. W., Magnus, B., Stucky, B. D., Liu, Y., Quinn, H., Thissen, D., . . . DeWalt, D. A. (2014). Psychometric properties of the PROMIS (R) pediatric scales: precision, stability, and comparison of different scoring and administration options. *Qual Life Res, 23*(4), 1233-1243. doi: 10.1007/s11136-013-0544-0

Veehof, M. M., Oskam, M. J., Schreurs, K. M. G., & Bohlmeijer, E. T. (2011). Acceptance-based interventions for the treatment of chronic pain: A systematic review and meta-analysis. *Pain, 152*(3), 533-542. doi: 10.1016/j.pain.2010.11.002

Vowles, K.E., & McCracken, L. M. (2008). Acceptance and values-based action in chronic pain: a study of treatment effectiveness and process. *Journal of Consulting and Clinical Psychology, 76*(3), 397-407.

Vowles, K.E., & McCracken, L. M. (2010). Comparing the role of psychological flexibility and traditional pain management coping strategies in chronic pain treatment outcomes. *Behaviour Research and Therapy, 48*(2), 141-146.

Vranceanu, A. M., Merker, V. L., Plotkin, S. R., & Park, E. R. (2014). The relaxation response resiliency program (3RP) in patients with neurofibromatosis 1, neurofibromatosis 2, and schwannomatosis: results from a pilot study. *J Neurooncol, 120*(1), 103-109. doi: 10.1007/s11060-014-1522-2

Walser, R, & Westrup, D. (2007). *Acceptance & Commitment Therapy for the Treatment on Post-Traumatic Stress Disorder & Trauma-Related Problems: A Practictioner's Guide to Using Mindfulness & Acceptance Strategies*. Oakland, CA: New Harbinger.

Weiss, H. R. (2003). Rehabilitation of adolescent patients with scoliosis--what do we know? A review of the literature. *Pediatric Rehabilitation, 6*(3-4), 183-194. doi: 10.1080/13638490310001636790 1X621E15JBUB6R5E [pii]

Wetherell, J. L., Afari, N., Rutledge, T., Sorrell, J. T., Stoddard, J. A., Petkus, A. J., . . . Hampton Atkinson, J. (2011). A randomized, controlled trial of acceptance and commitment therapy and cognitive-behavioral therapy for chronic pain. *Pain, 152*(9), 2098-2107. doi: S0304-3959(11)00339-3 [pii]10.1016/j.pain.2011.05.016

Wicksell, R. K., Dahl, J., Magnusson, B., & Olsson, G. L. (2005). Using acceptance and commitment therapy in the rehabilitation of an adolescent female with chronic pain: A case example. [Article]. *Cognitive and Behavioral Practice, 12*(4), 415-423.

Wicksell, R. K., Kemani, M., Jensen, K., Kosek, E., Kadetoff, D., Sorjonen, K., . . . Olsson, G. L. (2013). Acceptance and commitment therapy for fibromyalgia: a randomized controlled trial. *European Journal of Pain, 17*(4), 599-611. doi: 10.1002/j.1532-2149.2012.00224.x

Wicksell, R. K., Lekander, M., Sorjonen, K., & Olsson, G. L. (2010). The Psychological Inflexibility in Pain Scale (PIPS) - Statistical properties and model fit of an instrument to assess change processes in pain related disability. *European Journal of Pain, 14*, 771.e771-771.e714.

Wicksell, R. K., Melin, L., Lekander, M., & Olsson, G. L. (2009a). Evaluating the effectiveness of exposure and acceptance strategies to improve functioning and quality of life in longstanding pediatric pain - A randomized controlled trial. *Pain, 141*(3), 248-257. doi: 10.1016/j.pain.2008.11.006

Wicksell, R. K., Melin, L., Lekander, M., & Olsson, G. L. (2009b). Evaluating the effectiveness of exposure and acceptance strategies to improve functioning and quality of life in longstanding pediatric pain--a randomized controlled trial. *Pain, 141*(3), 248-257. doi: S0304-3959(08)00700-8 [pii] 10.1016/j.pain.2008.11.006

Wicksell, R. K., Melin, L., & Olsson, G. L. (2007). Exposure and acceptance in the rehabilitation of adolescents with idiopathic chronic pain - A pilot study. *European Journal of Pain, 11*(3), 267-274. doi: 10.1016/j.ejpain.2006.02.012

Wicksell, R. K., Olsson, G. L., & Hayes, S. C. (2011). Mediators of change in acceptance and commitment therapy for pediatric chronic pain. *Pain, 152*(12), 2792-2801. doi: 10.1016/j.pain.2011.09.003

Wolkenstein, P., Rodriguez, D., Ferkal, S., Gravier, H., Buret, V., Algans, N., . . . Bastuji-Garin, S. (2009). Impact of neurofibromatosis 1 upon quality of life in childhood: a cross-sectional study of 79 cases. *British Journal of Dermatology, 160*(4), 844-848. doi: 10.1111/j.1365-2133.2008.08949.x

Wolters, P., Burns, K.M., Martin, S., Baldwin, A., Dombi, E., Toledo-Tamula, M. A., . . . Widemann, B. (in press). Pain interference in youth with Neurofibromatosis Type 1 and plexiform neurofibromas and relation to disease severity, social-emotional functioning, and quality of life. *American Journal of Medical Genetics*.

Yuen, E. K., Herbert, J. D., Forman, E. M., Goetter, E. M., Juarascio, A. S., Rabin, S., . . . Bouchard, S. (2013). Acceptance based behavior therapy for social anxiety disorder through videoconferencing. *J Anxiety Disord, 27*(4), 389-397. doi: 10.1016/j.janxdis.2013.03.002

Zylowska, L., Ackerman, D. L., Yang, M. H., Futrell, J. L., Horton, N. L., Hale, T. S., . . . Smalley, S. L. (2008). Mindfulness meditation training in adults and adolescents with ADHD: a feasibility study. *J Atten Disord, 11*(6), 737-746. doi: 10.1177/1087054707308502

9 APPENDICES

9.1 APPENDIX A: SCREENING PHONE CALLS TO DETERMINE ELIGIBILITY

I) Introduction

- Hi, this is ______ calling from the NIH. I'm calling to tell you about a study we are conducting for people with NF1 and plexiform tumors who have chronic pain. Do you have a few minutes now to hear about the study?

II) ACT

- The study is investigating something called Acceptance and Commitment Training, or ACT. ACT is a type of therapy that focuses on things like values and living in the present moment. It has been found to be effective in helping people with other medical conditions cope with their pain, and we have a small amount of data in adolescents with NF1 that suggests it is helpful in reducing the amount that pain interferes with the person's life. The study would involve coming to the NIH two or three times over the course of a few months, and will also involve doing some of techniques in your day-to-day life at home. We are hoping that the ACT training will help people cope with their pain so that it has less impact on their life, and that it will improve people's quality of life. To thank participants for their time, we will be providing $30 each time you complete a set of baseline or follow-up questionnaires. You would get the money by check or direct deposit. Do you think you might be interested in hearing more about the study?
- If no: Thank you for your time.
- If yes: Okay, before I go into too much detail, let me ask you a few questions to see if you're eligible. This should take less than five minutes. If you want, I can email you these questions to read along with me. Would you prefer that? [If yes, email the questions and resume the call when they receive it.]

III) Screening

I'm going to ask you six questions about your pain. On a scale of 0 to 6, where 0 means not at all and 6 means completely, please think about the following questions:

	Has your pain:	Not at all			Some			Comp-letely
1.	made it difficult for you to do work (in or outside the home)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
2.	made it difficult for you to do activities outside of work (leisure activities)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
3.	made it difficult for you to spend time with friends and family members?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

4.	affected your mood?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
5.	affected your ability to do physical activities (like run, walk up stairs, play sports, do chores)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
6.	affected your sleep?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

Three or more items answered as "some"?	**Yes**	No
OR		
Mean score of 2.0 or above?	**Yes**	No

Okay, now just four more questions:

[Circle the patient's responses to the following questions:]

• How long have you had this pain? (≥ 3 months?)	**Yes** No
• Do you have access to a computer, tablet, or smartphone with internet capability?	**Yes** No
• Do you have any problems reading English?	Yes **No**
• Are you planning to start any other new studies for treating your pain or your tumors?	Yes **No**

- If **not** eligible: I'm sorry, but you are not eligible for the study because ______________. However, if you are interested, I can provide you with some online resources about ACT that you can read on your own.
- If eligible: Okay, these initial screening questions suggest that you are eligible for the study. Now I'll tell you a little more about it to see if you are interested.

IV) Procedures

- People who participate in this study will come to the NIH two to three times. The first time, you would come for about two days. During this visit:
    - Randomization – we will randomly assign people to the immediate intervention group or to the delayed intervention group.
    - All patients will:
        - Fill out questionnaires asking about pain, quality of life, emotional well-being
        - Get an electrocardiogram, or EKG – painless, to read heart rate
    - Immediate Intervention group –

    - This group will stay and do four hours of ACT Training (two 2-hour sessions) with a psychologist or psychology associate.
  - Delayed/Wait-list group –
    - Go home and do nothing different for two months, return for intervention after 8 weeks. During this time, if you were to start a new pain treatment or treatment study that might impact your level of pain, we would have to remove you from this study.

V) ACT Training

- You will learn some techniques that have been found effective for helping people deal with pain; ACT does not get rid of pain, it helps people change their relationship with their pain. In other words, instead of trying to fight your pain, we can talk about ways of living with your pain while focusing your energy on things that are most important to you. In this way, we try to help you have the best quality of life you can have, even while you have pain.
- You will continue to practice the ACT techniques at home:
  - Weekly emails – on an ACT-related topic with an assignment, something to practice during that week
  - Biweekly video chat sessions with a trainer to check on progress, continue to work on ACT techniques

VI) Follow-up

- All patients will return to the NIH after they complete the 8-week intervention:
  - Repeat questionnaires and EKG
- Final follow-up 6 months later from home
  - Repeat questionnaires from home computer
- To thank you for your time, we will be providing participants with a small amount of money each time they complete the follow-up questionnaires. We will also cover the costs of travel and some meals during your visits.

VII) Patient Interested?

Does this sound like something you would be interested in?

If no: Thank you for your time.

If yes: Okay, great! Let's try to find some possible dates when you could come for your first visit (ask about any upcoming surgeries that we may need to schedule around).

If eligible and interested, find possible dates for first visit:

9.2 APPENDIX B: ADULT BACKGROUND INFORMATION FORM

ADULT BACKGROUND INFORMATION FORM

(To be completed by adult participants at baseline)

Name:_________________________________ Date:___________ Date of Birth:___________

Phone Numbers: Home _______________ Work _______________ Cell _________________

Email: ______________________________ Do you prefer: ☐ Skype ☐ Facetime ☐ Other: ___________

Demographics

Sex: ☐ Male ☐ Female

Race: ☐White ☐African American/Black ☐Asian ☐Native Hawaiian/Pacific Islander ☐Unknown ☐American Indian/Alaskan Native

Ethnicity: ☐Hispanic or Latino ☐ Not Hispanic or Latino ☐Unknown

Marital Status: ☐ Single ☐ Married ☐ Divorced ☐ Separated ☐ Widowed

Occupational Status:

Are you currently working? ☐No ☐Yes ☐ On disability If working, hours per week: ______

Occupation: ____

How long at current job? _______________

Are you currently in school (e.g., college, vocational school, taking a class)? ☐No ☐Yes

If yes, please specify:______________________ ___________________________________

Are you receiving/Did you receive any special educational accommodations? ☐No ☐Yes

Level of Independent Living:

☐ I take care of myself (i.e., cooking, cleaning, bathing, dressing) independently.
☐ I need some help taking care of myself.
☐ I live in residential care.
☐ Other (please specify:____)

Educational History

Highest grade level in school completed (1 – 12): ________ years
Years of college completed (1 – 4): ________ years
Years of graduate/professional school completed: ________ years

School Performance: High School: ☐Average ☐Above Average ☐Below Average
College: ☐Average ☐Above Average ☐Below Average ☐ Not applicable

Psychological/Neurological History

Have you been diagnosed with any of the following:

Attention Deficit: ☐No ☐Yes
Learning Disability: ☐No ☐Yes Specify type: ____________________________
Depression: ☐No ☐Yes
Anxiety: ☐No ☐Yes
Other psychiatric diagnosis: ☐No ☐Yes Specify diagnosis: ____________________________

9.3 APPENDIX C: ADULT PAIN QUESTIONNAIRE

(Self report form for 18+ years)

Pain Interference Index – Adult

Below you will find a list of questions about you and your pain. Please answer each question by circling a number between 0 and 6.

Please note that we are asking about your pain during the last week.

	Has your pain:	Not at all			Some			Comp-letely
1.	made it difficult for you to do work (in or outside the home)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
2.	made it difficult for you to do activities outside of work (leisure activities)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
3.	made it difficult for you to spend time with friends and family members?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
4.	affected your mood?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
5.	affected your ability to do physical activities (like run, walk up stairs, play sports, do chores)?	**0**	**1**	**2**	**3**	**4**	**5**	**6**
6.	affected your sleep?	**0**	**1**	**2**	**3**	**4**	**5**	**6**

Adapted by the Neurobehavioral Group, NCI (8/23/13)

9.4 APPENDIX D: PAIN INTERFERENCE –SHORT FORM 8A -ADULT

PROMIS Item Bank v1.0 – Pain Interference – Short Form 8a

Pain Interference – Short Form 8a

Please respond to each question or statement by marking one box per row.

	In the past 7 days…	**Not at all**	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
1	How much did pain interfere with your day to day activities?	☐	☐	☐	☐	☐
2	How much did pain interfere with work around the home?.....................................	☐	☐	☐	☐	☐
3	How much did pain interfere with your ability to participate in social activities?	☐	☐	☐	☐	☐
4	How much did pain interfere with your household chores?....................................	☐	☐	☐	☐	☐
5	How much did pain interfere with the things you usually do for fun?..................	☐	☐	☐	☐	☐
6	How much did pain interfere with your enjoyment of social activities?..................	☐	☐	☐	☐	☐
7	How much did pain interfere with your enjoyment of life?....................................	☐	☐	☐	☐	☐
8	How much did pain interfere with your family life?..	☐	☐	☐	☐	☐

Participant Format Page 1 of 1

9.5 APPENDIX E: PAIN INTERFERENCE –SHORT FORM 8A –PEDIATRIC

PROMIS® Pediatric Item Bank v.1.0 - Pain Interference - Short Form 8a

Pediatric Pain Interference - Short Form

Please respond to each item by marking one box per row.

In the past 7 days…..

		Never	**Almost Never**	**Sometimes**	**Often**	**Almost Always**
3793R1	I had trouble sleeping when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
1698bR1	I felt angry when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2035R1	I had trouble doing schoolwork when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
9004	It was hard for me to pay attention when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2045R1	It was hard for me to run when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2049R1	It was hard for me to walk one block when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
1703R1	It was hard to have fun when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4
2180R1	It was hard to stay standing when I had pain.	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4

9.6 APPENDIX F: PEDSQL NEUROFIBROMATOSIS TYPE 1 MODULE

Neurofibromatosis Type 1: QOL instrument- Pediatric

DIRECTIONS

This survey is for individuals with NF 1. Neurofibromatosis type 1 sometimes causes special problems. Please tell us **how much of a problem** each one has been for you during the **past ONE month** by circling:

0 if it is **never** a problem

1 is it is **almost never** a problem

2 if it is **sometimes** a problem

3 if it is **often** a problem

4 if it is **almost always** a problem

There are no right or wrong answers.

If you do not know an answer, take your best guess.

Thank you for your help!

In the past **ONE month**, how much of a **problem** has this been for you…

PHYSICAL FUNCTIONING **(problems with…)**	**Never**	**Almost never**	**Some-times**	**Often**	**Almost Always**
1. Feeling physically weak	**0**	**1**	**2**	**3**	**3**
2. Walking more than one block	**0**	**1**	**2**	**3**	**3**
3. Climbing stairs	**0**	**1**	**2**	**3**	**3**
4. Running	**0**	**1**	**2**	**3**	**3**
5. Doing a sports activity or exercise	**0**	**1**	**2**	**3**	**3**

6. Lifting something heavy	**0**	**1**	**2**	**3**	**3**
7. Doing chores around the house	**0**	**1**	**2**	**3**	**3**

In the past **ONE month**, how much of a **problem** has this been for you…

DAILY ACTIVITIES (problems with…)	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Putting on shoes	**0**	**1**	**2**	**3**	**4**
2. Buttoning my shirt	**0**	**1**	**2**	**3**	**4**
3. Combing my hair	**0**	**1**	**2**	**3**	**4**
4. Getting into the bathroom to use the toilet	**0**	**1**	**2**	**3**	**4**
5. Undressing to use the toilet	**0**	**1**	**2**	**3**	**4**
6. Getting in and out of bathtub or shower	**0**	**1**	**2**	**3**	**4**
7. Brushing my teeth	**0**	**1**	**2**	**3**	**4**
8. Eating with a fork or knife	**0**	**1**	**2**	**3**	**4**
9. Using a phone	**0**	**1**	**2**	**3**	**4**
10. Shopping	**0**	**1**	**2**	**3**	**4**
11. Managing money	**0**	**1**	**2**	**3**	**4**
12. Driving	**0**	**1**	**2**	**3**	**4**

Neurofibromatosis Type 1: QOL instrument- Adult

DIRECTIONS

This survey is for individuals with NF 1. Neurofibromatosis type 1 sometimes causes special problems. Please tell us **how much of a problem** each one has been for you during the **past ONE month** by circling:

0 if it is **never** a problem

1 is it is **almost never** a problem

2 if it is **sometimes** a problem

3 if it is **often** a problem

4 if it is **almost always** a problem

There are no right or wrong answers.

If you do not know an answer, take your best guess.

Thank you for your help!

In the past **ONE month**, how much of a **problem** has this been for you…

PHYSICAL FUNCTIONING **(problems with…)**	**Never**	**Almost never**	**Some-times**	**Often**	**Almost Always**
1. Feeling physically weak	**0**	**1**	**2**	**3**	**3**
2. Walking more than one block	**0**	**1**	**2**	**3**	**3**
3. Climbing stairs	**0**	**1**	**2**	**3**	**3**
4. Running	**0**	**1**	**2**	**3**	**3**
5. Doing a sports activity or exercise	**0**	**1**	**2**	**3**	**3**
6. Lifting something heavy	**0**	**1**	**2**	**3**	**3**

7. Doing chores around the house	**0**	**1**	**2**	**3**	**3**

In the past **ONE month**, how much of a **problem** has this been for you…

DAILY ACTIVITIES (problems with…)	**Never**	**Almost Never**	**Some-times**	**Often**	**Almost Always**
1. Putting on shoes	**0**	**1**	**2**	**3**	**4**
2. Buttoning my shirt	**0**	**1**	**2**	**3**	**4**
3. Combing my hair	**0**	**1**	**2**	**3**	**4**
4. Getting into the bathroom to use the toilet	**0**	**1**	**2**	**3**	**4**
5. Undressing to use the toilet	**0**	**1**	**2**	**3**	**4**
6. Getting in and out of bathtub or shower	**0**	**1**	**2**	**3**	**4**
7. Brushing my teeth	**0**	**1**	**2**	**3**	**4**
8. Eating with a fork or knife	**0**	**1**	**2**	**3**	**4**
9. Using a phone	**0**	**1**	**2**	**3**	**4**
10. Shopping	**0**	**1**	**2**	**3**	**4**
11. Managing money	**0**	**1**	**2**	**3**	**4**
12. Driving	**0**	**1**	**2**	**3**	**4**

9.7 APPENDIX G: PAIN ANXIETY SYMPTOMS SCALE-20 (PASS-20)

Name: ______________________________ **Date:** _______________

PAIN ANXIETY SYMPTOMS SCALE-20 (PASS-20)

Individuals who experience pain develop different ways to respond to that pain. We would like to know what you do and what you think about when in pain. Please use the rating scale below to indicate how often you engage in each of the following thoughts or activities. Circle any number from 0 (NEVER) to 5 (ALWAYS) for each item.

		NEVER					ALWAYS
1.	I think that if my pain gets too severe, it will never decrease	0	1	2	3	4	5
2.	When I feel pain I am afraid that something terrible will happen	0	1	2	3	4	5
3.	I go immediately to bed when I feel severe pain	0	1	2	3	4	5
4.	I begin trembling when engaged in activity that increases pain	0	1	2	3	4	5
5.	I can’t think straight when I am in pain	0	1	2	3	4	5
6.	I will stop any activity as soon as I sense pain coming on	0	1	2	3	4	5
7.	Pain seems to cause my heart to pound or race	0	1	2	3	4	5
8.	As soon as pain comes on I take medication to reduce it	0	1	2	3	4	5
9.	When I feel pain I think that I may be seriously ill	0	1	2	3	4	5
10.	During painful episodes it is difficult for me to think of anything else besides the pain	0	1	2	3	4	5
11.	I avoid important activities when I hurt	0	1	2	3	4	5
12.	When I sense pain I feel dizzy or faint	0	1	2	3	4	5
13.	Pain sensations are terrifying	0	1	2	3	4	5
14.	When I hurt I think about the pain constantly	0	1	2	3	4	5
15.	Pain makes me nauseous (feel sick)	0	1	2	3	4	5
16.	When pain comes on strong I think I might become paralyzed or more disabled	0	1	2	3	4	5
17.	I find it hard to concentrate when I hurt	0	1	2	3	4	5
18.	I find it difficult to calm my body down after periods of pain	0	1	2	3	4	5
19.	I worry when I am in pain	0	1	2	3	4	5
20.	I try to avoid activities that cause pain	0	1	2	3	4	5

9.9 APPENDIX H: CENTER FOR EPIDEMIOLOGICAL STUDIES-DEPRESSION SCALE (CES-D

Name: ______________________________ **Date:** _______________

CES-D

Please indicate how often you have felt this way during the last week.

3 = Most or all of the time (5 to 7 days a week).

2 = Occasionally or a moderate amount of time (3 to 4 days a week).

1 = Some or a little of the time (1 to 2 days a week).

0 = Rarely or none of the time (less than once a week).

1. I was bothered by things that usually don't bother me.	0	1	2	3
2. I did not feel like eating: my appetite was poor.	0	1	2	3
3. I felt that I could not shake off the blues.	0	1	2	3
4. I felt that I was just as good as other people.	0	1	2	3
5. I had trouble keeping my mind on what I was doing.	0	1	2	3
6. I felt depressed.	0	1	2	3
7. I felt that everything I did was an effort.	0	1	2	3
8. I felt hopeful about the future.	0	1	2	3
9. I thought my life had been a failure.	0	1	2	3
10. I felt fearful.	0	1	2	3
11. My sleep was restless.	0	1	2	3
12. I was happy.	0	1	2	3
13. I talked less than usual.	0	1	2	3
14. I felt lonely.	0	1	2	3
15. People were unfriendly.	0	1	2	3
16. I enjoyed life.	0	1	2	3
17. I had crying spells.	0	1	2	3
18. I felt sad.	0	1	2	3
19. I felt that people disliked me.	0	1	2	3
20. I could not get going.	0	1	2	3

9.10 APPENDIX I: NUMERIC RATING SCALE-11 (NRS-11)

I am going to ask you two questions about how much your plexiform neurofibroma tumor hurts.

First, where is the location of your most important tumor pain?
(Specify the location of that tumor:____).

Below are lines with numbers from 0 to 10 where 0 means no pain and 10 means the worst pain you can imagine.

1. Please circle the one number that best describes that most important tumor pain at its **worst** during the past week.

0 1 2 3 4 5 6 7 8 9 10
No pain — Worst pain you can imagine

2. Please circle the one number that best describes your overall tumor pain at its **worst** during the past week.

0 1 2 3 4 5 6 7 8 9 10
No pain — Worst pain you can imagine

9.11 APPENDIX J: CHRONIC PAIN ACCEPTANCE QUESTIONNAIRE (CPAQ)

P - CPAC

CPAQ

Directions: Below you will find a list of statements. Please rate the truth of each statement as it applies to you. Use the following rating scale to make your choices. For instance, if you believe a statement is 'Always True,' you would write a 6 in the blank next to that statement.

0	1	2	3	4	5	6
Never True	Very rarely true	Seldom true	Sometimes true	Often true	Almost always true	Always true

1. ______I am getting on with the business of living no matter what my level of pain is.
2. ______My life is going well, even though I have chronic pain.
3. ______It's OK to experience pain.
4. ______I would gladly sacrifice important things in my life to control this pain better.
5. ______It's not necessary for me to control my pain in order to handle my life well.
6. ______Although things have changed, I am living a normal life despite my chronic pain.
7. ______I need to concentrate on getting rid of my pain.
8. ______There are many activities I do when I feel pain.
9. ______I lead a full life even though I have chronic pain.
10. ______Controlling pain is less important than any other goals in my life.
11. ______My thoughts and feelings about pain must change before I can take important steps in my life.
12. ______Despite the pain, I am now sticking to a certain course in my life.
13. ______Keeping my pain level under control takes first priority whenever I'm doing something.
14. ______Before I can make any serious plans, I have to get some control over my pain.
15. ______When my pain increases, I can still take care of my responsibilities.
16. ______I will have better control over my life if I can control my negative thoughts about pain.
17. ______I avoid putting myself in situations where my pain might increase.
18. ______My worries and fears about what pain will do to me are true.
19. ______It's a relief to realize that I don't have to change my pain to get on with my life.
20. ______I have to struggle to do things when I have pain.

Scoring: Chronic pain acceptance questionnaire

Activities engagement: Sum items 1, 2, 3, 5, 6, 8, 9, 10, 12, 15, 19

Pain willingness: Reverse score items 4, 7, 11, 13, 14, 16, 18, 18, 20 and sum

Total: activity engagement + pain willingness

9.12 APPENDIX K: PSYCHOLOGICAL INFLEXIBILITY IN PAIN SCALE (PIPS)

Below you will find a list of statements. Please rate how true each statement is for you right now by circling a number next to it.

1	**2**	**3**	**4**	**5**	**6**	**7**
Never true	Very rarely true	Seldom true	Sometimes true	Often true	Almost always true	Always true

1. I cancel planned activities when I am in pain. **1 2 3 4 5 6 7**
2. I say things like “I don’t have energy”, “I am not well enough”, “I don’t have time”, “I don’t dare”, “I have too much pain”, “I feel too bad”, or “I don’t feel like it”.
   1 2 3 4 5 6 7
3. I need to understand what is wrong in order to move on. **1 2 3 4 5 6 7**
4. Because of my pain, I no longer plan for the future. **1 2 3 4 5 6 7**
5. I avoid doing things when there is a risk it will hurt or make things worse.
   1 2
   3 4 5 6 7
6. It is important to understand what causes my pain. **1 2 3 4 5 6 7**
7. I don’t do things that are important to me to avoid pain. **1 2 3 4 5 6 7**
8. I postpone things because of my pain. **1 2 3 4 5 6 7**
9. I would do anything to get rid of my pain. **1 2 3 4 5 6 7**
10. It’s not me that controls my life, it’s my pain. **1 2 3 4 5 6 7**
11. I avoid planning activities because of my pain **1 2 3 4 5 6 7**
12. It is important that I learn to control my pain. **1 2 3 4 5 6 7**

9.13 APPENDIX L: LIFE EVENTS CHECKLIST

Name:_____________________________ Date:____________________

Please place a checkmark next to the events that **<u>you</u>** have experienced during the **past 6 months.**

_____ 1. Birth or adoption of a sibling by parent

_____ 2. Marriage of a parent

_____ 3. Divorce of parents

_____ 4. Marital separation of parents

_____ 5. Death of a grandparent

_____ 6. Close family member leaving home for an extended period

_____ 7. Loss of job by parent

_____ 8. Financial hardship (e.g., difficulty paying bills)

_____ 9. Family gets financial assistance

_____ 10. Death of a parent

_____ 11. Death of a sibling

_____ 12. Death of a peer

_____ 13. Move to a new school/college/job

_____14. Repeated a grade or college course

_____ 15. Suspension from school/college

_____ 16. Decline in school grades or work performance

_____ 17. Significant number of school/work absences (16 or more)

____ 18a Hospitalization

18b Please specify # of days:

___ 1-5 ___6-10 ___11-15 ___16+

18c Reason hospitalized:_________________________

____ 19a Hospitalization of your parent

19b Please specify # of days:

___ 1-5 ___6-10 ___11-15 ___16+

____ 20. Discovery of a family member's serious illness

____ 21. Discovery of a serious illness (please specify:________________________)

____ 22. Disclosure of diagnosis to others

____ 23. One or more changes in residence

____ 24. Family member experiencing problems with drugs or alcohol

_____25. Substantial change in peer group

_____26. Teased in school/college

____ 27. Problems with school administration

____ 28. Teacher reporting behavior problems in school/college

____ 29. Other stressful event occurring in family

Please specify _________________________________.

____ 30. Experienced a change in primary caregiver(s).

Please specify _________________________________.

____ 31. Parent has serious medical condition.

Please specify _________________________________.

____ 32. Giving birth or adopting a child

_____33. Getting married

_____34. Separated from spouse or significant other

_____35. Divorced

_____36. Death of your spouse

_____37. Death of your child

_____38. Experiencing legal issues

_____39. Experiencing stress related to a serious illness

_____40. Discovery of a serious illness for your child

_____41.a Hospitalization of your child

41.b Please specify # of days
___ 1-5 ___6-10 ___11-15 ___16+

_____42. Loss of job

_____43. Other stressful event related to work or school.

Please specify ________________________________.

☐ Check here if <u>none</u> of the above events have occurred in your life in the past 6 months.

Please take a few seconds to make sure you have reviewed <u>every</u> item on page 1 and page 2. Thank you for filling out this form!

9.14 APPENDIX M: PAIN MANAGEMENT INVENTORY

Pain Management Inventory

(1) In the past month, have you taken any medication for your pain? Yes No
If no, skip to question (2). If yes, please provide the following information:

Medication 1: Name ______________________ Dose _______________

How often do/did you take this medication? (check one)

☐ Less than once a month ☐ 1-3 times a month ☐ Once a week ☐ 2-4 times a week ☐ Daily

Medication 2: Name ______________________ Dose _______________

How often do/did you take this medication? (check one)

☐ Less than once a month ☐ 1-3 times a month ☐ Once a week ☐ 2-4 times a week ☐ Daily

(2) In the past month, have you done any behavioral techniques <u>for the purpose of managing your pain</u> besides ACT (for example, yoga, relaxation, exercise)? Yes No

If yes, please list and provide the following information:

1: Name ___________________________

How often do you do this?

☐ Less than once a month ☐ 1-3 times a month ☐ Once a week ☐ 2-4 times a week ☐ Daily

2: Name ___________________________

How often do you do this?

☐ Less than once a month ☐ 1-3 times a month ☐ Once a week ☐ 2-4 times a week ☐ Daily

(3) In the past month, have you done any other techniques <u>for the purpose of managing your pain</u>? Yes No

If yes, please list and provide the following information:

Name ___________________________

How often do you do this?

☐ Less than once a month ☐ 1-3 times a month ☐ Once a week ☐ 2-4 times a week ☐ Daily

9.15 APPENDIX N: PAIN MANAGEMENT INVENTORY

Pain Management Inventory – 6 month follow-up

(1) In the past month, have you taken any medication for your pain? Yes No

If no, skip to question (2). If yes, please provide the following information:

Medication 1: Name ______________________ Dose _______________
How often do/did you take this medication? (check one)

☐	☐	☐	☐	☐
Less than once a month	1-3 times a month	Once a week	2-4 times a week	Daily

Medication 2: Name ______________________ Dose _______________
How often do/did you take this medication? (check one)

☐	☐	☐	☐	☐
Less than once a month	1-3 times a month	Once a week	2-4 times a week	Daily

(2) In the past month, have you done any behavioral techniques <u>for the purpose of managing your pain</u> besides ACT (for example, yoga, relaxation, exercise)? Yes No

If yes, please list and provide the following information:

1: Name ___________________________
How often do you do this?

☐	☐	☐	☐	☐
Less than once a month	1-3 times a month	Once a week	2-4 times a week	Daily

2: Name ___________________________
How often do you do this?

☐	☐	☐	☐	☐
Less than once a month	1-3 times a month	Once a week	2-4 times a week	Daily

(3) In the past month, have you done any other techniques for the purpose of managing your pain? Yes No

If yes, please list and provide the following information:

Name ________________________

How often do you do this?

☐ Less than once a month
☐ 1-3 times a month
☐ Once a week
☐ 2-4 times a week
☐ Daily

(4) In the past SIX months, have you had any new treatments (e.g., surgeries, alternative therapies) for your NF1? Yes No

If yes, please specify: ______________________________________

Date of Treatment: _______________________

9.17 APPENDIX O: ACT INVENTORY

1. In the past month, how often have you engaged in the following strategies? (choose *only one* response)

a. Mindfulness (e.g., mindful breathing, responding mindfully to your pain)

☐ Not at all	☐ 1 – 2 times	☐ Once a week	☐ 2 – 3 times a week	☐ Daily

b. Noticing that your thoughts about your pain are just thoughts, and not judging them

☐ Not at all	☐ 1 – 2 times	☐ Once a week	☐ 2 – 3 times a week	☐ Daily

c. Doing something you wanted to do even though you were in pain

☐ Not at all	☐ 1 – 2 times	☐ Once a week	☐ 2 – 3 times a week	☐ Daily

d. Listening to your mindfulness CD (or downloaded audio)

☐ Not at all	☐ 1 – 2 times	☐ Once a week	☐ 2 – 3 times a week	☐ Daily

e. Reading ACT materials (e.g., online or in your workbook)

☐ Not at all	☐ 1 – 2 times	☐ Once a week	☐ 2 – 3 times a week	☐ Daily

2. In the past month, when have you engaged in strategies taught in the study? (*check all* that apply)

☐ Never	☐ When I remember	☐ When I have pain	☐ When I am upset	☐ Daily

3. How much did you like doing this study?

☐ Not at all	☐ Just A Little	☐ Some	☐ Pretty Much	☐ A Lot

4. How helpful did you find the in-person ACT training sessions at the NIH?

☐ Not at all	☐ Just A Little	☐ Some	☐ Pretty Much	☐ A Lot

5. How many of the weekly emails did you read?

☐ None	☐ A few (1 or 2)	☐ About half (3-5)	☐ Most (6 or 7)	☐ All (8)

6. How helpful did you find the weekly emails?

☐	☐	☐	☐	☐
Not at all	Just A Little	Some	Pretty Much	A Lot

7. How helpful did you find the video chat sessions?

☐	☐	☐	☐	☐
Not at all	Just A Little	Some	Pretty Much	A Lot

9.18 APPENDIX P: GLOBAL IMPRESSION OF CHANGE SCALE

Name: ____________________________ Date: ________________

Think about how much pain interferes with your life currently. Compared to when you first started this study, would you say this is:

☐ 1 Very Much Improved
☐ 2 Much Improved
☐ 3 Minimally Improved
☐ 4 No Change
☐ 5 Minimally Worse
☐ 6 Much Worse
☐ 7 Very Much Worse

References: Guy, 1976; Farrar et al., 2001 (DOI: 10.1016/S0304-3959(01)00349-9).

9.19 APPENDIX Q: ACT WORKBOOK

ACT WORKBOOK

Psychology Group
Behavioral Health Core
National Institutes of Health

Noticing Your Pain

Write down any thoughts that come up when you think about your worst pain.

What Have you Tried?

What have you tried to get rid of your pain? What do you do when your pain is bad?

Mindfulness in Our Daily Lives

1. Mindfulness in Your Morning Routine

Pick an activity that is part of your morning routine, like brushing your teeth, eating breakfast, or taking a shower. When you do it, totally focus on what you're doing – the way your body moves, the taste, the touch, the smell, the sound, and so on. Notice what is happening with an attitude of being open and curious.

For example, when you are brushing your teeth, notice the feel of the toothbrush in your hand. Notice the smell of the toothpaste and what it looks like as you squeeze some onto your brush. Notice the way it feels in your mouth, and as you brush along your front teeth, back teeth, gums, and tongue. Notice the sound of the brush going up and down or side to side in your mouth. Notice the sound of the running water, and how it feels to spit into the sink.

2. Mindfulness of Domestic Chores

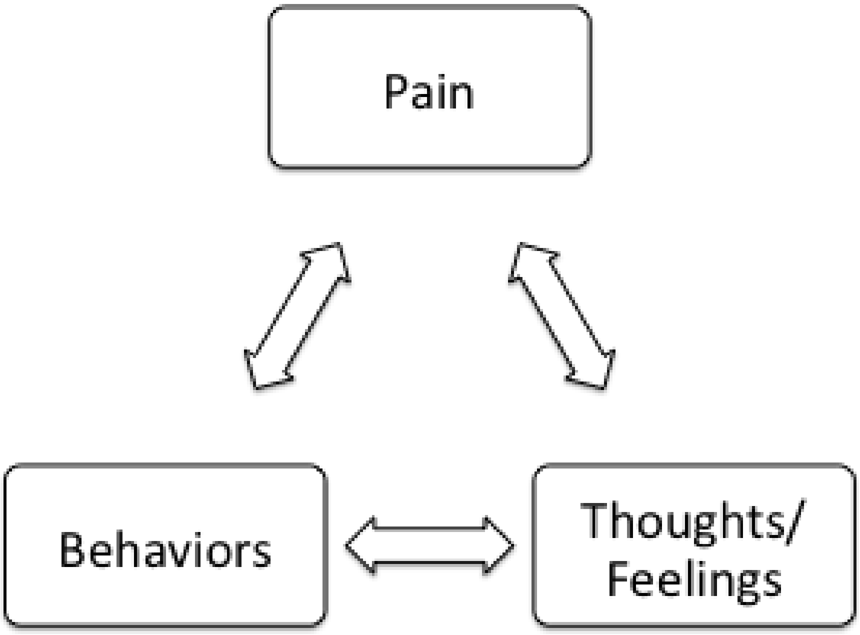
Pick one of your chores, like making your bed, cooking, or setting the table, and do it mindfully. For example, when making your bed, notice the color and shape of the pillows, and the pattern made by the creases in the sheets. Notice the feel of the bedspread in your hands as you pull it up, and the movement of your arms and shoulders and hands.

If you feel yourself being bored or frustrated, just notice it and then bring your attention back to what you're doing. Again and again, your attention will wander. As soon as you realize this has happened, gently notice it, and then bring your attention back to what you are doing.

3. Mindfulness of Pleasant Activities

Pick an activity that you enjoy, such as listening to music, eating lunch, stroking the cat, playing with the dog, walking in the park, having a soothing hot bath, and so on. Do this activity mindfully – engage in it fully, using all five of your senses, and enjoy every moment. If and when your attention wanders, as soon as you realize it, notice what distracted you, and re-engage in whatever you are doing.

Adapted from Act Made Simple by Russ Harris.


Pain
Behaviors
Thoughts/
Feelings

Examples of Defusion Metaphors

When you notice a distressing or unpleasant thought, visualize…

- placing the thought on a leaf floating by on a stream
- the words scrolling by on a computer screen
- cars passing on the street outside your window
- the words printed on a sign, being held by people walking by in a parade
- placing the thought on a cloud as it slowly drifts through the sky

Which image do you like the best?

End of day 1:
Keep Going…

** Take a walk.* Walk around the neighborhood (or clinical center, Inn) with the goal being just to talk a walk. Focus on internal sensations (your feet as they touch the ground, the way your arms swing back and forth) and external stimuli (sounds of birds chirping or traffic, breezes). Avoid talking to others.

* *Mindfulness Exercise.* Do mindful breathing or a body scan for 5 minutes tonight.

Values Assessment

Value	**Importance 1-10**	**Success 1-10**
Education/learning/personal growth		
Employment		
Friendship/social		
Recreation/hobbies		
Spirituality/religion		
Community		
Health/physical well-being		
Couples/intimate relationship		
Family		

Tips for Setting Goals

Goals should be SMART:

Specific: Specify the actions you will take, when and where you will do so, and who or what is involved. A non-specific goal is: “I will spend more time with my family.” A specific goal is “I will go for a walk with my sister on Saturday morning.”

Meaningful: The goals should be personally meaningful to you. If it is genuinely guided by your values then it will be meaningful.

Adaptive: Does the goal help you take your life forwards in a direction that, as far as you can predict, is likely to improve the quality of your life?

Realistic: The goals should be realistically achievable. Take into account your health, competing demands on your time, financial status, and whether you have the skills to achieve it.

Time-bound: To increase the specificity of the goal, set a day, date and time for it. If this is not possible, set as accurate a time limit as you can.

Goals Form

Step 1: Write one of your values here: ______________________________________

Step 2: Think about goals you can set for yourself that will help you live more consistently with the value indicated above.

Step 3: Write some goals below:

* An Immediate Goal (something small, simple, easy, I can do in the next 24 hours)

* Short-term Goals (things I can do over the next few days and weeks)

* Medium-term Goal(s) (things I can do over the next few weeks and months)

* Long-term Goal(s) (things I can do over the next few months and years)

____

Step 1: Write one of your values here: ______________________________________

Step 2: Think about goals you can set for yourself that will help you live more consistently with the value indicated above.

Step 3: Write some goals below:

* An Immediate Goal (something small, simple, easy, I can do in the next 24 hours)

* Short-term Goals (things I can do over the next few days and weeks)

* Medium-term Goal(s) (things I can do over the next few weeks and months)

* Long-term Goal(s) (things I can do over the next few months and years)

Facing Barriers – Part 1

Choose one of your goals from the goals form that you think you may have difficulty with and write it here:

____

Now write down the possible barriers that may arise that could prevent you from accomplishing this goal:

1. ____

2. ____

3. ____

4. ____

Now ask yourself two questions:
Are you willing to have those barriers show up and still move towards your goal?
(If not, practice expansion or re-evaluate your goals/values)

and

What will you do when barriers arise?

Recruiting Others: Sample Script

You are very important to me, and I really need your support right now. I have set some goals for myself that will help me live according to my values. I realize that it is normal and okay to have pain. I understand that it's hard for you to see me in pain and to encourage me to do things when I'm really down or in pain. It would mean a lot to me if you would do it anyway, like a coach. I will care about you no matter what, but I really want to do some important things and you can help me with this. Are you willing to support me in my values and goals, even when it's hard for you? This is what I want for my life.

9.20 APPENDIX R: PRACTICE EXERCISES

Continue Practicing At Home!!

Mindfulness Exercises: Simple Ways to Get Present

Take Ten Breaths This is a simple exercise to center yourself and connect with your environment. Practice it throughout the day, especially any time you find yourself getting caught up in your thoughts and feelings.
1. Take ten slow, deep breaths. Focus on breathing out as slowly as possible until the lungs are completely empty—and then allow them to refill by themselves.
2. Notice the sensations of your lungs emptying. Notice them refilling. Notice your rib cage rising and falling. Notice the gentle rise and fall of your shoulders.
3. See if you can let your thoughts come and go as if they're just passing cars, driving past outside your house.
4. Expand your awareness: simultaneously notice your breathing and your body. Then look around the room and notice what you can see, hear, smell, touch, and feel.

Drop Anchor This is another simple exercise to center yourself and connect with the world around you. Practice it throughout the day, especially any time you find yourself getting caught up in your thoughts and feelings.
1. Plant your feet into the floor.
2. Push them down—notice the floor beneath you, supporting you.
3. Notice the muscle tension in your legs as you push your feet down.
4. Notice your entire body—and the feeling of gravity flowing down through your head, spine, and legs into your feet.
5. Now look around and notice what you can see and hear around you. Notice where you are and what you're doing.

Notice Five Things This is yet another simple exercise to center yourself and engage with your environment. Practice it throughout the day, especially any time you find yourself getting caught up in your thoughts and feelings.
1. Pause for a moment
2. Look around and notice five things that you can see.
3. Listen carefully and notice five things that you can hear.
4. Notice five things that you can feel in contact with your body (for example, your watch against your wrist, your trousers against your legs, the air on your face, your feet upon the floor, your back against the chair).
5. Finally, do all of the above simultaneously

There are many poems, books, songs, TV shows, and movies where you can find ACT-related concepts. For example, the following poem illustrates the concept of mindfulness.

When Singing, Just Sing – Life as Meditation

When sitting, just sit.
When eating, just eat.
When walking, just walk.
When talking, just talk.
When listening, just listen.
When looking, just look.
When touching, just touch.
When thinking, just think.
When playing, just play.
And enjoy the feeling of each moment and each day.

by Narayan Liebenson Grady

See if you can notice other examples of ACT themes you might see or hear!

Other Ways to Practice ACT in Your Life

** Take 10.* Set the alarm on your watch or cell phone to go off 2 times during the next hour. If you don't have an alarm, write a note on a small piece of paper that you carry around or put somewhere visible to remind you. When you hear the alarm or notice the paper, stop what you are doing and take 10 seconds to pay attention to what is going on around you and within you.

* Search online for "mindfulness bell". You can set a timer so that a bell rings periodically to remind you to slow down, get centered, and <u>notice</u>.

* Wear a particular piece of jewelry or put a small sticker or pin on your wallet or purse. Let this be your "values" symbol. It could also be a photo of a special person in your life (like your child or partner). Choose a value (a thing or person) that you want it to represent, then try to think of that value every time you see the symbol. Let it remind you of how important that value is to you, and encourage you to do something to move toward that value today.

References and Resources

Books

Get Out of Your Mind and Into Your Life: The New Acceptance and Commitment Therapy
By Steven Hayes

Mindfulness for Beginners: Reclaiming the Present Moment and Your Life

By Jon Kabat-Zinn

ACT Made Simple: An Easy-to-Read Primer on Acceptance and Commitment Therapy
By Russ Harris

CDs/Downloads/Audio

Mindfulness Meditation for Pain Relief: Guided Practices for Reclaiming Your Body and Your Life

By Jon Kabat-Zinn

Websites

http://www.actmindfully.com.au/

http://www.acceptandchange.com/audio/

http://www.drluoma.com/actresources.html#materials

http://julianmcnally.com/Content/psychological-services/

9.21 APPENDIX S: VIDEO CHAT MANUAL

Video chat Sessions

Session 1 (week 2)

Committed Action

- Ask patient about their thoughts, impressions, etc. since the in-person sessions. What have the last two weeks been like? Discuss content of weekly email briefly.
- Ask about any difficulties that have come up – focus on willingness; challenge of sitting with, or acknowledging those difficult thoughts and feelings in the service of their values.
- Remind them to practice mindful breathing – ask about how that is going.
- Check in on goals; what short-term goals did they accomplish? Do they need help adjusting any goals?
- Revisit concept of committed action and what they are willing to have in order to live a valued life.
- Use metaphors, exercises from in-person sessions as reminders, as necessary…i.e., "How tightly are you holding that thought?" "Thank your mind for that thought," "Invite that thought to be present when you move towards your values."

Session 2 (week 4)

Noticing Progress

- Ask patient about their progress – how do they feel they have been doing? What has gotten in the way? What positive changes have they noticed, if any? Discuss content of weekly email briefly.

Ideas to explore:

- Sometimes we are so wrapped up in thinking about moving from one goal to the next that we forget to notice how much we have accomplished. Help patient take a minute to really notice any changes s/he might be experiencing and the progress made so far. (See if they can come up with behaviors they have engaged in that are associated with one or more of their values)
- Take a moment to really focus on that sense of accomplishment. What comes up…pride? Satisfaction? Frustration that it wasn't more? What does that (pride) feel like to you? See if you can sit with that feeling for 20 seconds, just noticing it without doing anything else.
- Some people have a hard time with this…if this is the case, explore why: Is it that you haven't taken the time to notice what's going on with your emotions or behavior? They don't understand some of the concepts?

- Clarify any questions the patient has about any of the concepts they are struggling with.

Session 3 (week 6)

Self-compassion and Review of Committed Action

- How have the techniques you have learned been working in other areas of your life besides pain? Ask for examples…relationships, work, school, leisure time, etc. Discuss content of weekly email briefly.

- Revisit goals. Discuss progress, and set specific goals for them to work on between now and their return visit.

- Often people with pain tend to experience anger or frustration related to various pain-related challenges:
  - Why can't I control my pain better?
  - Why can't I learn to cope better?
  - Resentment at family members or others who "don't understand what it's like", and guilt for feeling that way
  - Anger at doctors for not making it better

- Explore ideas of:
  - Connecting with others with chronic pain (and NF, and PNs)
  - Forgiveness and kindness exercises (pgs 274-278, Radical Acceptance)
    - Select phrases that resonate in the moment
    - Say the phrase out loud
  - Allowing the anger to be there but not letting it control us
    - Connect with the idea that the anger (or other distressing thoughts and emotions) are usually there to *try to* protect you (not always helpful!)
  - Recognizing the impermanence of waves of anger, sadness, anxiety, and even physical pain

- Cultivating self-compassion in our daily lives – instead of continuing to be on auto-pilot, how do we remember to practice mindfulness and self-care?

- How self-compassion can help keep us on track towards values (re-establish committed action)

Weekly E-mails

Week One

Noticing Your Thoughts

We talked before about how our minds are sometimes helpful, like when they remind us that we need to get to work or school on time. We also talked about the fact that our minds are not so helpful sometimes.

Now that you are back home, have you noticed any thoughts your mind has had about this study? Maybe your mind has said, "This ACT stuff is crazy!" or "It might work for other people, but it's never going to work for me!" Or maybe your mind has told you that it *is* going to work – right away! It might be saying "Hurry up and feel better!"

If your mind has been telling you anything similar to these thoughts, it certainly makes sense. All of those thoughts are understandable and normal. The important thing is that you NOTICE the thoughts (that's being mindful), and just let them come and go (that's acknowledging). Maybe even thank your mind for those thoughts, and then choose how to behave based on your VALUES!

Take about 30 seconds right now to reflect on the above paragraphs, and then read on for your weekly activities…

This week:

1) Focus on one of the goals you set for yourself when we met at the NIH that you can work on this week. When you are working towards that goal, remind yourself of the value to which it's related. You might say to yourself, "I am doing this because ________." Fully acknowledge how it feels to work towards something you truly value.

2) Write that same value down on a piece of paper and put it somewhere in your house where you will see it every morning, like on your dresser or taped to your mirror, to help you remember it. Every time you notice it, really think about how important that value is to you. See if this makes it easier to reach your goal!

Week Two

Be Mindful When Doing…Anything!

We have talked a lot about mindfulness. Being mindful and aware of our thoughts and feelings can help us remain focused on our values and remind us to move towards our goals. Actually, we can be mindful while doing pretty much anything. For example, when you get dressed in the morning which foot do you put into your pants first? You probably don't remember because it's something you do without thinking about it. If you were to practice mindfulness while getting dressed, you would notice all sorts of things that you usually miss. You might notice the feel of the fabric of your pants as you pick them up and how your body adjusts to balance on one foot. You might notice how soft the fabric is against your skin or how the buttons on your shirt are really pretty. Imagine how much more you could experience if you actually paid attention to these things!

This week:

Practice being mindful when you are going through your daily routine. Notice the thoughts that pop into your mind. Say to yourself "I'm noticing my mind having this thought," or "I notice that my body feels _______." The things you notice could be pleasant, like "I notice the sun feels nice and warm on my face." Or they could be unpleasant, like "I notice my head starting to hurt." Whatever you notice, practice paying attention to what you are experiencing in the moment!

And remember to practice your mindful breathing! ☺

Week Three

Getting Some Perspective

Now that you are several weeks into the program, what are your thoughts? Feelings? Have you noticed any differences in any areas of your life?

This week, let's review how we can be aware of our thoughts but not let them change how we act and what we do. We spend so much time THINKING, that sometimes it's easy to forget that our thoughts aren't always right or in control. For example, if you have the thought "I'm a banana," does that make you a banana? Of course not! Go ahead and try it: say to yourself "I'm a banana." Now look down…are you still you? I'm guessing the answer is yes! Just like having the thought "I can't reach my goal" doesn't mean that you actually can't reach your goal.

There are lots of ways we can practice having thoughts without acting on them. We can look at the thoughts in a different way or from a different perspective. Here's an example:

Imagine that you are in the woods near a stream. As you're sitting next to the stream enjoying the moment, thoughts may come up. You may think about a TV show that you watched last night or what you have to do at work or school tomorrow. Or you may start thinking about your pain. You may think, "I'd like to stay here, but I am in pain." When these thoughts come up, they can pull you out of the current moment. If you're thinking only about your pain then you're not enjoying the calming nature setting.

We might be able to get a different perspective by changing one word in the above thought. Let's change BUT to AND. So now, we can say "I'd like to stay here, AND I am in pain." Does that change the meaning? Just slightly, but yes! Now you have a choice. This may help you realize that you can be in pain AND continue to enjoy sitting by the stream.

Other examples:

(1) "I need to call my friend back, but I'm tired," becomes "I need to call my friend back, AND I'm tired."

(2) "I'd like to read a book to my child, but I have a headache," becomes "I'd like to read a book to my child, AND I have a headache."

In each case, you can choose what to do next based on your values, not based on the pain.

This week:

1) Look for opportunities this week to change a "but" to an "and". When you start to tell yourself you are unable to do something because of your pain, see if you can re-word that thought so you have a CHOICE. "I'd like to do X, AND I am noticing some pain." Then make a choice about what to do next. Whatever you choose, make sure the choice comes from your values, not your pain.

2) Find a quiet space where you can practice this activity for five minutes. When you are settled into a comfortable position, think about your pain and notice any feelings that come up. Where in your body are they located? Do you feel it in your head, your jaw, your shoulders? Some people might feel a tightness in their chest, or butterflies in their stomach, or sweaty palms… Next, picture yourself breathing in and around that sensation in your body. Take a few deep breaths. Now picture yourself creating extra space in your body, opening up that area to make room for the feeling to move freely. Finally, allow the feeling to be there even though you may not like it or want it. Softly say to the feeling, "I notice you. You are my guest. You are welcome to stay here with me in this moment."

Week Four

Revisiting Goals

Have you thought about the fact that, by signing up for this study, you are doing something to make positive changes in your life? Traveling to the NIH, filling out all those forms, reading all these emails, having those video chat sessions – all of it is to help you move closer to your values. Not all people make that kind of effort, so take a minute to notice why you are doing all of this. Sometimes, when we start something new to improve our lives, we end up doing too much too soon. We may set a goal for ourselves that ends up being too big. For example, if one of your values is art, you may decide your goal is to paint a picture to hang on your wall. If you already know how to pain, this may be fine. But for someone who is just starting out, it may take a while to reach that goal. In that case, the best thing to do may be to set some smaller goals along the way. You might first set the goal of studying various art techniques. You could look at art books, get some art supplies, even sign up for an art class. Maybe you set one of those goals for each week. When you have accomplished those goals, you will be much closer to reaching your long-term goal of painting that picture!

Remember the following steps for realistic goal-setting:
1) If you lack skills, set new goals around learning them.
2) If your goal is too big, break it down into small chunks.
3) If you don't have the things you need in order to reach your goal, think about how you can get them or whom you can ask for help.
4) If you feel like you don't have enough time to reach your goal, ask yourself what you are willing to give up in order to make time.
5) If the goal is truly impossible, like because of health problems, lack of money, or other problems you cannot control, then set a different one that is more realistic.

This week:

Remember all the values you identified when you were at the NIH? Take out your workbook and look at the ratings you gave yourself (page 7). Using a different color ink (or different mark), rate yourself again on each of those values, thinking about the progress you have made so far.
Now review the goals you set for yourself. Have you reached any of them? If not, think about how you can break the goal into smaller parts. Write those down. If you have reached one or more goals, check that off and then focus on the next one.

We will be talking via video chat soon!

Week Five

Many Ways to Say Our Thoughts

On page 2 of your workbook, you wrote down some thoughts that you sometimes notice about your pain. Pick one of those thoughts now, and try the following ten steps:

1. Say the thought out loud.
2. Say it again in slow motion.

3. Say it as fast as you can.
4. Say it standing on one foot.
5. Say it jumping up and down.
6. Say it in a high, squeaky voice.
7. Say it in a low voice.
8. Say it while trying not to move your lips.
9. Sing it to the tune of Happy Birthday.
10. Say it with a British accent.

Do you notice anything about how you felt saying it in the beginning compared to how you felt at the end of those ten statements? There is no right or wrong reaction. The point is just to notice what comes up as you go through the ten statements.

This week:

When you notice any thoughts that your mind hands you about your pain or your goals, try saying them out loud using some of the ten ideas above. If you're around other people, you can even do it inside your head. Then notice how you feel afterwards.

Week Six

Writing About Your Values

We are at week 6! How did your assignment go last week? Were you able to say any thoughts about your pain in a funny or different voice? How did it go? At the very least, did you laugh at how silly it might have seemed? It can be a very different experience, reciting words or thoughts in that way!

Here is a question for you: since you started this study, how much have you been thinking about your values? Has it been more or less than before the study? Have you noticed anything else in relation to thinking about your values? Have you felt any differently? There is no right or wrong answer. It just may be something to consider.

Interestingly, researchers have discovered that there are health benefits from writing about life goals and values. So that is what your assignment is this week. We can talk about how you did when we talk on video chat, but you do not have to share anything specific that you wrote about unless you want to!

This week:

Use a blank page in your workbook, a journal (if you have one), or just a spare piece of paper. Spend ten minutes writing about one of your values. For example, try writing about:
a) why the value is important to you
b) things you have done that support this value
c) things you would like to do to continue supporting the value
d) anything else that comes to mind.

If you find that you are still writing at the end of the 10 minutes, feel free to continue! Remember, you don't have to share what you have written with anyone if you don't want to. This is just for you.

Week Seven

Commitment

Do you realize that you only have a couple more weeks of this training program? We talked before about one thing that can help us reach our goals - our commitment. In other words, how sure are we that we are going to stick with the program? One way we can help our commitment stay strong is to get encouragement and support from other people. Have you talked to other people about your goals and values? Is anyone in your life cheering you on and helping you reach those goals? Is there anyone close to you who shares one of your values?

There are a lot of ways that other people can show their support. They might check in with you every week about your progress, or do a goal-related activity with you, or just listen when you need to talk. Having someone on your side can help you stay motivated and on track!

This week:

1) Think about a person who has supported you during this study so far. This can be a friend, parent, brother or sister, other relative, boyfriend/girlfriend, spouse, coach, or teacher. If you have felt encouraged by their support, tell them that! It can be something as simple as "Thank you for helping me work on these goals." Or you could do something nice for that person to show him or her how much their support means to you.
If you could use a little extra support, ask for it gently. You may say something like "Your support means a lot to me. One way you could help me work towards my goal is to ___________."
2) As a bonus activity, you could then ask that person if there is anything you can do to help them on one of their goals! If you are able to do something nice for that person, think about how good it feels to help the people we care for. Does that relate to one of your values?

Week Eight

Don't Stop Now!

Congratulations – you are at the final week of the training program!

This first part of the study is almost over. Think about what you've accomplished during the past 8 weeks. Have you reached any of your short-term goals? Have you been practicing mindfulness? How have these activities helped you in terms of the values that are important to you? Do you feel any different – physically or emotionally – than when you started the program?

If you have been working towards your goals, you should take a moment to congratulate yourself on your hard work! And although you may have been able to check some goals off of your list, hopefully you want to keep living in support of your values. Just because you're almost done with the ACT training program doesn't mean we want you to stop what you're doing! Goals help us to work towards those values, but *as long as we're living, we're never done living our values*.

So take some time to evaluate the progress you've made so far and give yourself credit for all your hard work. At the same time, keep striving to live your values, and think about what steps you can take to continue leading a more valued life.

This week:

Consider what you can do in the coming weeks and months to help you live a valued life. You may be ready to set some new goals. Think of a long-term goal and 3 short-term goals that you can work on next. Remember, the most important thing about any goals that you set is that they should be related to one of the things that matter the most to you.
Come up with your own long and short-term goals based on your values, and keep living those values every day! Let's discuss your ideas during our upcoming visit at the NIH.

9.23 APPENDIX S: ACCEPTANCE AND COMMITMENT THERAPY CORE COMPETENCY SELF-RATING FORM

Below are listed a number of statements. Please rate how true each statement is for you when you use ACT, by circling a number next to it. Use the scale below to make your choice.

1	2	3	4	5	6	7	*?*
never true	very seldom true	seldom true	sometimes true	frequently true	almost always true	always true	*don't know*

Core Competencies Involved in the Basic ACT Therapeutic Stance

The basic psychological stance of the ACT therapist is an especially important factor in providing good treatment. This involves being able to make contact with the "space" from which ACT naturally flows, as well as modeling certain facets of psychological flexibility that we seek to impart to the client. Like many treatment traditions, ACT emphasizes the importance of therapist warmth and genuineness. This stance emerges quite naturally from the core understanding of human suffering from an ACT perspective. When we see our clients trapped by language, we see ourselves and the traps which generate our own pain. An "I and thou" perspective is the natural precipitant of this recognition. Collectively, the following attributes define the basic therapeutic stance of ACT.

1	The therapist realizes that he or she is in the same soup as the client and speaks to the client from an equal, vulnerable, genuine, and sharing point of view	☐
2	The therapist models willingness to hold contradictory or difficult ideas, feelings, memories, and the like without needing to "resolve" them.	☐
3	The therapist takes a compassionate and humanizing stance toward the client's suffering and avoids criticism, judgment or taking a "one up" position	☐
4	The therapist always brings the issue back to what the client's experience is showing, and does not substitute his or her opinions for that genuine experience	☐
5	The therapist does not argue with, lecture, coerce or even attempt to convince the client of anything. If you find yourself attempting to change a client's mind, stop. You are not doing ACT.	☐
6	The therapist does not explain the "meaning" of paradoxes or metaphors to develop "insight"	☐
7	The therapist is willing to self disclose about personal issues when it makes a therapeutic point	☐
8	The therapist avoids the use of "canned" ACT interventions. Interventions are responses to the particular client we are treating.	☐
9	The therapist tailors interventions to fit the client's language and immediate life experience	☐
10	The therapist sequences and applies specific ACT interventions in response to client needs, and is ready to change course to fit those needs at any moment	☐

11	New metaphors, experiential exercises and behavioral tasks are allowed to emerge from the client's own experience and context	☐
12	ACT relevant processes are recognized in the moment and where appropriate are directly supported in the context of the therapeutic relationship	☐

Developing Acceptance and Willingness/Undermining Experiential Control

13	Therapist communicates that client is not broken, but is using unworkable strategies	☐
14	Therapist helps client examine direct experience and detect emotional control strategies	☐
15	Therapist helps client make direct contact with the paradoxical effect of emotional control strategies	☐
16	Therapist actively uses concept of "workability" in clinical interactions	☐
17	Therapist actively encourages client to experiment with stopping the struggle for emotional control and suggests willingness as an alternative.	☐
18	Therapist uses shifts between control and willingness as an opportunity for the client to directly experience the contrast in vitality between the two strategies.	☐
19	Therapist helps client investigate relationship between levels of willingness and sense of suffering willingness suffering diary; clean and dirty suffering)	☐
20	Therapist helps client make experiential contact with the cost of being unwilling relative to valued life ends (Are you doing your values; listing out value, emotional control demand, cost, short term/long term costs and benefits)	☐
21	Therapist helps client experience the qualities of willingness (a choice, a behavior, not wanting, same act regardless of how big the stakes)	☐
22	Therapist uses exercises (jumping; cards in lap, eye contact) and metaphors (box full of stuff, Joe the bum) to help client contact willingness the action in the presence of difficult material	☐
23	Therapists structures graded steps or exercises to practice willingness	☐
24	Therapist models willingness in the therapeutic relationship	☐
25	Therapist detects struggle in session and teaches the clients to do so	☐

Undermining Cognitive Fusion

26	Therapist identifies client's emotional, cognitive, behavioral or physical barriers to willingness	☐
27	Therapist suggests that "attachment" to the literal meaning of these experiences makes willingness difficult to sustain	☐
28	Therapist actively contrasts what the client's "mind" says will work versus what the client's experience says is working	☐
29	Therapist uses language tools (get off our buts, both/and), metaphors (bubble on the head, two computers, monsters on the bus) and experiential exercises (tin can monster) to create a separation between the client and client's conceptualized experience	☐
30	Therapist uses various interventions to both reveal the flow of private experience and such experience is not "toxic"	☐
31	Therapist works to get client to experiment with "having" these experiences, using willingness as a stance	☐
32	Therapist uses various exercises, metaphors and behavioral tasks to reveal the "hidden" properties of language (milk, milk, milk; what are the numbers?)	☐
33	Therapist helps client elucidate the client's "story" and helps client make contact with the arbitrary nature of causal relationships within the story	☐
34	Therapist helps client make contact with the evaluative and reason giving properties of the client's story (no thing matters, good cup/bad cup)	☐
35	Therapist detects "mindiness" (fusion) in session and teaches the client to detect it as well	☐

Getting in Contact with the Present Moment

36	Therapist can defuse from client content and direct attention to the moment	☐
37	Therapist can bring his or her own feelings or thoughts in the moment into the therapeutic relationship	☐
38	Therapist uses exercises to expand the clients sense of experience as an ongoing process	☐
39	Therapists tracks content at multiple levels and emphasizes the present when it is useful	☐
40	Therapist models coming back to the present moment	☐
41	Therapist detects client drifting into past and future orientation and comes back to now	☐

42	Therapists teaches the client to do likewise	☐

Distinguishing the Conceptualized Self from Self-as-context

43	Therapist helps the client differentiate self-evaluations from the self that evaluates (thank your mind for that thought, calling a thought a thought, naming the event, pick an identity)	☐
44	Therapist employs mindfulness exercises (the you the you call you; chessboard, soldiers in parade/leaves on the stream) to help client make contact with self-as-context	☐
45	Therapist uses metaphors to highlight distinction between products and contents of consciousness versus consciousness (furniture in house, are you big enough to have you)	☐
46	The therapist employs behavioral tasks (take your mind for a walk) to help client practice distinguishing private events from self	☐
47	Therapist helps client understand the different qualities of self conceptualization, just noticing events and simple awareness	☐

Defining Valued Directions

49	Therapist helps client clarify valued life directions (values questionnaire, value clarification exercise, what do you want your life to stand for, funeral exercise)	☐
50	Therapist helps client “go on record” as wanting to stand for valued life ends	☐
51	Therapist puts his or her own therapy relevant values in the room and models their importance	☐
52	Therapist teaches clients to distinguish between values and goals	☐
53	Therapist distinguishes between outcomes and processes	☐
54	Therapist respects client values and if unable to support them, finds referral or other alternatives	☐

Building Patterns of Committed Action

55	Therapist helps client identify valued life goals and build an action plan	☐
56	Therapist encourages client to “have” barriers and make and keep commitments	☐

57	Therapist uses exercise and non traditional uses of language to reveal hidden sources of interference to committed actions (fish hook metaphor, forgiveness, who would be made right, how is your story every going to handle you being healthy)	☐
58	Therapist encourages client to take small steps and to look at the quality of committed action	☐
59	Therapist keep clients focused on larger and larger patterns of action	☐
60	Therapist integrates slips or relapses into the experiential base for future effective action	☐

9.25 APPENDIX T: TREATMENT FIDELITY CHECKLIST

Session 1

Technique/Concept	Presented/Discussed
Creative Hopeless – discussion of how pain impacts the patient's life, what they have avoided or given up	
Mindfulness exercise(s) in session with follow-up discussion of patient's perceptions, reactions	
Avoidance versus Acceptance – with discussion of how willingness to experience pain is essential for living a valued life	
Use of metaphor/experiential exercises (e.g., Tug-of-war, Index card exercise) to demonstrate concepts	
Self-compassion – imagery exercise and/or discussion of how lack of self-compassion can negatively impact emotional well-being	
Out-of-session practice – Assign exercises to work on before Session 2	

Session 2

Technique/Concept	Presented/Discussed
Values Assessment – help patient identify values; do values imagery exercise	
Completion of Values Rating Form	
Values vs. Goals	
Completion of Goal-setting Form for at least two values	
Dealing with Obstacles – choice point/swamp metaphor	
Enlisting support – discussion of how important others can support their pursuit of valued living	
Review workbook for at-home practice	

9.27 APPENDIX U: ACT MANUAL

SESSION ONE

Overview of sessions • This treatment is for people who have NF1 and PNs, and chronic pain. • Today's session: about two hours, with a break about half way through • We will be talking about how pain impacts your life, about some of the main concepts in Acceptance and Commitment Training, or ACT, and about how these can be useful for people with chronic pain. **Confidentiality** • Psychologists are bound by limits to confidentiality; by law, we have to report if we think you are a danger to yourself or someone else, or if we learn about a situation involving child abuse.	2 minutes
Define ACT • Purpose of ACT is to help people live a full and meaningful life with the pain that goes with it. • You may not be able to change your pain, but you can change your relationship with your pain. • There are a number of central concepts in ACT, and over these two sessions we'll go through them all. • Many things we'll talk about and ideas I'll ask you to consider might seem strange, and that's okay. I'm not asking you to believe anything I say. I'm just asking you to participate fully and see what happens.	3 minutes
How does pain impact your life? • How does pain impact your life? What areas of your life would be different if you didn't have pain? Work? School? Relationships? Others? • What thoughts come up when you think about your worst pain? [Workbook pg 2] • What have you tried to get rid of your pain? How do you try to avoid pain? What has worked in the long term? [Establish creative hopelessness.] [Workbook pg 2]	10 min
Our minds: helpful or harmful? • Basic functions of our minds. They help us think, reason, feel, behave a certain way, etc. When we talk about our thoughts, we are going to refer to our "minds" as being where our thoughts come from. Sometimes our minds are helpful, and sometimes they are not. Our minds have evolved to try to tell us when there's danger, they tell you if something is good or bad for you, and they'll talk about the same things over and over. • When our minds are not helpful: What does your mind say to you if you make a mistake? [Discuss how things our minds say can make us feel or act a certain way.]	2 minutes
Mindfulness	3 minutes

• Mindfulness means "Noticing what's going on around you and inside you with flexibility, openness, and curiosity." • Discuss impact of not being mindful or aware of what we do or feel in the moment. • Examples of "mindlessness" – auto-pilot, sleepwalking…Finishing a meal and realizing that you barely remember eating it, getting to the end of a paragraph and not remembering anything you read. Sometimes your thoughts will go back to the past or something that may happen in the future, and so you end up missing out on the present. • Why is mindfulness important? It helps us be more aware of everything going on within and around us so that when we react, we do so with clarity and purpose. • How does someone become more mindful? It's as simple as breathing…	
Mindfulness Exercise • Part 1: Mindfulness of Breath – notice your breathing as you inhale and exhale. Don't try to change it, just remain aware. If you get distracted, gently bring your focus back to your breath. (Purpose is not to relax, just to notice). • Part 2: Notice any thoughts about this study, about what you're missing at home or work, anything else that comes up. Visualize letting those thoughts sit with you in the room while you're here, but not letting them take over. Connect with what value led you to be here. • Brief discussion of person's experience.	10 minutes
Mindfulness At Home (workbook page 3) • Morning Routine • Mindfulness of Domestic Chores • Mindfulness of Pleasant Activities	5 minutes
Acknowledgement (the opposite of avoidance) • Acknowledging one's pain means having an attitude that your situation is real and believable without trying to change what cannot be changed. • Acknowledge thoughts about pain without judging them, reacting impulsively • Acceptance of your pain means that you believe it to be real and true, it does not mean you're giving up or that you like it. Wanting to get rid of the pain is natural, but that's different from actively struggling against it. • Tug-of-war metaphor – use rope to exemplify how we can pull against something for so long, but if we drop the rope we get out of the struggle easily.	10 minutes
Acceptance Exercise: Expansion • Expansion means giving yourself space to experience pain (physical or emotional pain). (1) Observe → What are the feelings/physical sensations that arise when you think about your worst pain? Notice them, where in your body is it located? (2) Breathe → Visualize yourself breathing into and around the sensation. (3) Create space → Imagine yourself creating extra space within your body, opening up to make room for the sensation to move freely. (4) Allow → Allow the sensation to be there even though you don't like or want it.	10 minutes

Practice this now. Discuss patient's experience: what was it like to <u>not</u> resist the pain? If the person says it was strange or difficult, reinforce the idea that they stuck with despite those thoughts…	
Relationship between thoughts, feelings, behaviors (workbook page 4) • Relationship between pain, thoughts/feelings, and behaviors: they each can impact the others, can become a vicious cycle. • Which of these three things do we have the most control over? • Chocolate Cake Metaphor - instruct patient to <u>not</u> think of chocolate cake for 10 seconds. [Illustrates lack of control over thoughts.] • Electric shock exercise – imagine you are hooked up to a machine that will deliver a painful shock if you feel any anxiety in the next minute. [Illustrates lack of control over feelings.] So our best bet is our <u>behavior</u>.	7 minutes
Break	5 minutes
Defusion • Another principle in ACT relates to what we call "holding thoughts lightly". This means stepping back and separating from our thoughts, images, and memories; seeing our thoughts for what they are – just words or pictures. Just because we have thoughts does not make them true. Some people who live with chronic pain have thoughts like "When I have pain I have to _________." [Ask patient to fill in the blank.] "Hold them lightly instead of clutching them tightly". • Card Exercise - Write down key phrases the patient uses to describe his/her pain on index cards. First talk about how pain can feel like it's right in front of your face. What's the problem with this? Can we have a conversation? • Next, toss the index cards toward the patient first instructing them to not let any land on them, then instructing them to let them land where they may. Notice the difference in the energy expended when you are fighting to keep your pain away versus accepting it. • Examples of other metaphors - Notice a thought, picture it, then put it on a leaf floating by on a stream. Words scrolling by on a computer screen. Cars passing by outside your window. Which one does the patient like best? (workbook page 5)	5 minutes
Distancing • Choose one thought the patient often has about their pain. Practice adjusting the content as follows: I can't stand this pain. I'm having the thought I can't stand this pain. I notice my mind having the thought I can't stand this pain. • Physically distancing oneself from "pain" – have person write "pain" (or a thought about their pain) on a piece of paper, then first stand on it, then take one step back, then another, noticing their experience. Discuss.	5 minutes
Pain Versus Values	15 minutes

• Are there times when your pain gets in the way of living according to your values? [discuss examples from client's life] • Examples: (1) It is important to spend time with my friends, but there are times when I stay home or avoid group activities because of my pain. (2) My education/career is important, but I sometimes don't go to class/work because I am in pain. • Show picture of two identical circles – one surrounded by small circles, one by large circles. Discuss idea that the first one looks bigger. Those center circles are to represent pain. What fills the outer circles…values. Fill in the circles together. Why do those outer circles get so small sometimes? • A → B → C Review ABC model where A = activating event, B = behavior, C = consequence. Discuss examples where consequences are missing out on valued activities.	
Body Scan. • Review each part of the body, starting with feet, then legs, abdomen, chest, arms, neck, head. Ask patient to notice sensations in each body part without judging.	10 minutes
Slowing Things Down • Discuss slowing down the interaction between A and B. Creating space here through mindfulness, acknowledging…[Give examples]	5 minutes
Self-compassion • Acknowledging that living with chronic pain is not easy; sometimes others don't understand, can be unkind, sometimes our minds are unkind as well. • What are some examples of things our minds say to us that are unkind? When our minds tell us these things, how do we feel inside? When have others made things more difficult? • Imagery exercise: Imagine yourself as a young child of 5 or 6 years old. Imagine the child asking you for what he/she needed then. If you had one minute to tell them something helpful, what would it be? Imagine giving the child compassion. [Discussion.]	10 minutes
Out-of-Session Assignments *1) Talk a walk.* Walk around the neighborhood (or clinical center, Inn) with the goal being just to talk a walk. Focus on internal sensations (your feet as they touch the ground, the way your arms swing back and forth) and external stimuli (sounds of birds chirping or traffic, breezes). Avoid talking to others. 2) *Mindfulness exercise.* Do a body scan or mindful breathing for 5 minutes.	3 minutes

SESSION TWO

Checking In Ask about experiences doing the Mindfulness exercises last night. Thoughts about Session 1.	5 minutes
Values Assessment • We need our minds to help us do some things, but other times it is important to use something else to guide us: VALUES – the things that are most important to us, what we want our life to be about. ACT is based on the idea that the key to leading a fulfilling life is defining your values and acting on them. • Discuss question: What are you willing to have in order to live a valued life?	10 minutes
What Do You Want Your Life To Stand For exercise *(can be brief or longer depending on how well the person is in touch with values)* • Imagine you are at your next milestone birthday party. You are listening to people get up and talk about you, the kind of person you are, your parents, your siblings, your friends, your children, etc. What would you like those people to say about you? Imagine them saying exactly what you would most want them to say. [If participants have a hard time thinking of values, ask them to name someone they admire and talk about the particular qualities s/he admires.]	5 minutes
Values Compass • Workbook page 7: Discuss areas where you might have certain values. For example, in the "community" area, you might have values related to a certain group you're involved with in the community (a charity or club at school that does community service). Trainer can gently encourage a focus on the areas most impacted by pain, if patient is ready for that. • Make distinction between values and goals. • Rate each one (1-10) on how close patient is living in accordance with those values. • Importance of moving just one point in the valued direction.	15 minutes
Goal-setting • Discussion of Values vs. Goals • Introduce Goals Form and have patient start filling it out. [Workbook page 9] • Complete form together for at least two values.	20 minutes
Demons on the Boat • As you've thought about your goals, one thing you might notice (or may notice soon) is that your minds might start up again, telling you all kinds of not-helpful things, like "You can't do that!" or "You've tried that before and it never works." • When this happens, it can be helpful to think about something we call "Demons on the Boat." Explain metaphor – those thoughts sometimes come up right when we're making progress, but are we willing to have them and still move towards our goal?	5 minutes

Break	5 minutes
How to Deal With the Obstacles • Swamp metaphor/Choice point guided exercise: You start out towards your goal of reaching a desired place but soon find yourself having to trudge through a muddy swamp to get there. What do you do? • Imagine it both ways…turning around and going home, or moving forward. What feelings and thoughts show up? [Discuss reactions] • Review Facing Barriers exercise [workbook page 14]	10 minutes
Enlisting Support and Addressing Conflicts • How to deal with conflicts with other people in our lives about practicing ACT techniques at home; how to enlist their support. • Sample script [workbook page 15] • Ultimately we may have to accept others' lack of acceptance.	5 minutes
Generalizing Techniques • How patients can apply these techniques to other areas of their life, other problems related to their NF (learning disabilities, visible tumors, etc) • Ask patient to share other areas of his/her life besides pain that cause challenges or difficulties – start with other aspects of NF, but anything is okay. • Help them come up with ACT techniques that are applicable.	15 minutes
Worries Moving Forward • Ask participants to name any worries they might be having about how they will do once they get back home and into their normal routine. • On index card: Write down fears and take the card with them. Emphasize that they can move forward even while having doubts. Also, they are not committing to be successful in every attempt they make. But each time they do not accomplish a goal, they need to re-commit to try again.	5 minutes
Final Mindfulness Exercise • With each breath in, visualize breathing in compassion for yourself as you make space for the awareness that you will falter, you will trip up, and run into obstacles when you try to apply these techniques at home. Your breath is taking in an acceptance of that awareness and a gentle reminder for you to be kind and compassionate to yourself when that happens. With each breath out, breathe out kindness and warmth to others that are with you on your journey, your partners, friends, families, teachers, and breathe out an awareness that they will mess up as well, so with each exhale, you're noticing the need to be compassionate towards them when that happens.	5 minutes
Wrap-up • Workbooks have additional exercises to continue working at home. • Discuss weekly emails again and biweekly video chat sessions.	5 minutes

9.28 APPENDIX V: RECRUITMENT E-MAILS

9.28.1 NCI Patient E-mail

Dear Sir or Madam:

We are emailing you because you indicated on the CTF Registry that you are willing to be notified about research studies. There is a new study at the National Cancer Institute evaluating an intervention to help people cope with chronic pain related to plexiform neurofibroma tumors. The intervention is called Acceptance and Commitment Training, or ACT. It has been found to be effective in many studies of people with pain who have other medical conditions. A small study by our group suggests that it may be helpful for people with NF1 as well because it decreased how much pain interfered with people's daily lives.

For this new study, people will be asked to come to the NIH for a 2-day visit. During this visit, they will fill out some questionnaires that ask about things like pain severity and emotional well-being. They also will get an electrocardiogram (ECG), which is a painless procedure that monitors heart rate. Next, we will randomly select (like flipping a coin) half of the people to do the ACT training right away. The other half will be put on a wait list for two months, and then return to the NIH to do the training.

There are three parts to the training. First, you will participate in two 2-hour sessions with an ACT trainer at the NIH during which you will learn new ways of coping with pain. Second, you will receive weekly emails for 8 weeks, each about ways you can work on ACT techniques at home. Third, you will have three video chat sessions (such as Skype, done on your home computer at week 2, week 4, and week 6) with your ACT trainer.

At the end of the 8-week training, we will ask everyone to return to the NIH to complete questionnaires again and get another ECG. Six months later, we will ask you to complete the questionnaires one last time from your home computer.

To be eligible, you must be between 16 and 59 years of age, have one or more plexiform neurofibromas, and have chronic pain for at least the past three months. You also must be able to read and speak English, and have regular access to a computer with internet access. Individuals ages 16 and 17 years must have a parent or guardian give permission for their participation.

The NIH will offer some reimbursement for travel and expenses for people who live more than 50 miles away. Also, all participants will receive a small monetary gift to thank you for your time each time you complete a set of questionnaires (3 to 4 times total).

To learn more about the study, please contact Associate Investigator Taryn Allen, PhD (240-760-6001, taryn.allen@nih.gov) or the study's Principal Investigator, Staci Martin, PhD., (240-760-6025, martins@mail.nih.gov). We will be able to tell you more about the study requirements and find out if you are eligible.

9.28.2 Recruitment E-mail CTF Registry

Dear Sir or Madam:

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At the end of the 8-week training, we will ask everyone to return to the NIH to complete questionnaires again and get another ECG. Three months later, we will ask you to complete the questionnaires one last time from your home computer.

To be eligible, you must be between 16 and 59 years of age, have one or more plexiform neurofibromas, and have chronic pain for at least the past three months. You also must be able to read and speak English, and have regular access to a computer with internet access. Individuals ages 16 and 17 years must have a parent or guardian give permission for their participation.

The NIH will offer some reimbursement for travel and expenses for people who live more than 50 miles away. Also, everyone will receive a small monetary gift to thank you for your time each time you complete a set of questionnaires.

To learn more about the study, please contact Taryn Allen, PhD, at 240-760-6001 (taryn.allen@nih.gov) or the study's Principal Investigator, Staci Martin Peron, PhD., at 240-760-6025, or email her at martins@mail.nih.gov. We will be able to tell you more about the study requirements and find out if you are eligible.

9.29 APPENDIX W: RECRUITMENT FLYER

Coping with Pain:
an ACTive Approach

NATIONAL CANCER INSTITUTE®

- ✓ Do you have NF1 and one or more plexiform neurofibromas?
- ✓ Do you have pain that has lasted three months or more?
- ✓ Are you between the ages of 16 and 59 years?

If you answered yes to all these questions, you may be eligible for a new study at the National Cancer Institute in Bethesda, Maryland.

The study is evaluating an intervention called **Acceptance and Commitment Training**, or **ACT**, which has been found effective in other medical populations for decreasing how much pain interferes with daily life.

Funding is available to cover travel and lodging costs, and participants are paid to thank them for their time.

To learn more about the study, please contact:

Dr. Taryn Allen 240-760-6001 taryn.allen@nih.gov	or	Dr. Staci Martin 240-760-6025 martins@mail.nih.gov

ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025	ACT for Pain Dr. Staci Martin 240-760-6025