

**Individualized Assessment and Treatment Program for TMD:
Coping as a Mechanism
(TMD 3c)
Research Protocol**

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SPECIFIC AIMS

Temporomandibular disorders (TMD) are a group of painful conditions that affect a large number of otherwise healthy adults. The purpose of this proposal is to employ an Experience Sampling (ES) procedure to study TMD pain episodes in near real-time, and to use that information to design a coping-skills based treatment that will be tailored to each patient's specific circumstances. We believe that this personalized approach to cognitive-behavioral treatment, **Individualized Assessment and Treatment Program (IATP)**, will more effectively build adaptive coping skills and reduce catastrophization, and prove to be an effective and innovative treatment model. Psychosocial treatments have been partially effective for TMD, but the mechanisms of action for these treatments are unclear. We propose that one reason for these findings is that treatment, even cognitive-behavioral treatment (CBT), as normally delivered fails to adequately assess patient coping in pain episodes or to deliver effective skills training to manage those situations. In part, the lack of effectiveness is due to our limited ability to assess pain-related coping skills as they are actually used, and to teach those skills that are actually needed for a given individual. I.e., coping is vital, but poorly trained.

We propose to recruit 160 chronic TMD pain patients to test IATP for patients with TMD pain. Experience sampling (ES) via smartphone app at a rate of 4 randomly prompted records per day for a 2-wk monitoring period prior to the beginning of treatment will be used to gather information for a functional analysis of pain episodes based on patients' situation, momentary cognitions, affects, and coping behaviors. Therapists will use this information to work with the patient to develop adaptive coping tactics **tailored to that person** in a 6-session CBT program. Follow-ups will be conducted every 3mo out to 12mo.

Experience sampling during-treatment (at weeks 2 and 4) will allow adjustment of the treatment goals and procedures, making the treatment adaptive and able to change with changing circumstances and patient needs. This experimental treatment will be added to a standard conservative splint-based treatment for TMD pain (i.e., STD+IATP). The combination will be compared to a STD treatment plus a conventional cognitive-behavioral pain treatment (CBT), that does not employ individualized assessments (i.e., STD+CBT). In the STD+CBT condition experience sampling data will be collected, but will not be used to inform treatment. ES by STD+CBT patients will also control for measurement reactivity.

Specific aims are as follows:

1. To determine if STD+IATP yields lower pain and better adaptational outcomes than does a standard conservative treatment plus conventional CBT (STD+CBT).
H1: STD+IATP will result in lower pain and depressive symptoms, less interference with lifestyle in the long-term, and better quality of life than will the STD+CBT treatment.
2. A. To determine whether the addition of an Individualized Assessment and Treatment Program to Standard Treatment (STD+IATP) results in greater use of coping skills than does a standard conservative treatment plus conventional CBT (STD+CBT).
H2a: It is hypothesized that the highly relevant skills highlighted in IATP will result in significantly greater increases in reported use of coping skills from pre- to posttreatment relative to STD+CBT.
B. To determine if coping skills acquired in treatment are maintained in the STD+IATP condition, compared to the STD+CBT condition.
H2b: It is hypothesized that STD+IATP patients will continue to report increased use of coping skills relative to STD+CBT patients up to 12 months following treatment.
3. To determine specifically whether treatment-related improvements in mood, cognitions, self-efficacy and coping behaviors account for treatment outcomes. (I.e., does adaptive coping mediate treatment effects?).
H3: It is predicted that patients in the IATP condition will exhibit increased numbers of specific coping behaviors (e.g., relaxation), improved mood, higher self-efficacy for pain control, and decreased frequency and intensity of catastrophization as measured in real time, as compared to STD+CBT patients, and that these changes will mediate treatment outcomes.

The results will help indicate whether treatment can be made more effective, what classes of mechanisms need to be addressed to enhance treatment for TMD sufferers, and will evaluate the role of coping in accounting for improvement in TMD treatment. If these mechanisms can be successfully identified **and manipulated** on an individual basis it would have implications for the development of more effective treatment programs for TMD and for related disorders.

B. BACKGROUND AND SIGNIFICANCE

Epidemiological studies have indicated that up to 50% of the adult population has at least one sign of temporomandibular dysfunction/orofacial pain (TMD)(Manfredini et al., 2012). It is further estimated that between 5 and 12% of the population suffers from a serious TM dysfunction at some point in life (NIDCR, 2015). TMD is the second most common musculoskeletal condition (after chronic low back pain) resulting in pain and disability, and annual management costs in the USA, not including imaging, have doubled in the last decade to over \$4 billion (NIDCR, 2013).

Studies of the symptoms, course, and treatment of TMD indicate that the disorder shares much in common with headache and back pain. The disorder appears to be multiply determined, with both psychosocial and physical factors playing a role in the development and maintenance of the disorder (Flor & Turk, 2011; Harper, Schrepf, & Clauw, 2016). Although persistent pain is the cardinal feature of TMD, stress, depression, disability and dysfunctional illness are also significant aspects (Dworkin & Massoth, 1994). Also in common with headache and back pain is the finding that a variety of treatments, all presumably with different aims, have shown success with some patients.

A number of behavioral and psychological treatments have been used to treat TMD pain. Among these have been interpersonal psychotherapy (Pomp, 1974), biofeedback (Gardea, Gatchel, & Mishra, 2001), relaxation (Wahlund, Nilsson, & Larsson, 2015), hypnosis (Simon & Lewis, 2000; Zhang et al., 2015), and particularly cognitive-behavioral approaches (Dworkin et al., 1994; Litt, Shafer, & Kreutzer, 2010; Turner, Mancl, & Aaron, 2006). All of these treatment approaches have produced some success. Dworkin and Massoth (1994) reported that some improvement in symptomatology is reported in 85% of cases receiving a psychosocial intervention. The reasons for the success of behavioral or cognitive-behavioral programs are not clear, however. Turner et al. (1994) noted that nonspecific effects of treatment, plus disease natural history and regression to the mean, can result in high rates of good outcomes in pain treatments, “which may be misattributed to specific treatment effects” (p. 1609). Burns (2016) has suggested that different treatments may all be working through a few common mechanisms. *The true causes of improvements in pain after treatment will remain unknown in the absence of carefully designed studies that manipulate and evaluate mechanisms of treatment.*

Mechanisms of Treatment: Altering Pain Beliefs, Coping, Behaviors, and Mood States

Cognitive-behavioral treatments (CBT) presumably improve pain by decreasing maladaptive behaviors and cognitions (in particular, catastrophizing), and by increasing adaptive cognitions and coping (Turk et al., 1983; Turner & Romano, 2001). Relatively little research has been conducted to determine if cognitive-behavioral treatments actually lead to these kinds of changes, and if so, whether those changes are accounting for symptom reduction. Turner et al. (2007; 1995) provided some support for this mechanistic view. Patients in CBT reported better 1-year outcomes than those assigned to an education/attention control condition. The improvements were mediated by baseline to 6-mo changes in pain beliefs (particularly control over pain), catastrophizing, self-efficacy for managing pain, and particularly perceived control over pain. Measurement of coping behavior, however, was restricted to use of relaxation, which was not found to be influential. Similar findings were reported by Dura-Ferrandis et al. (2017), though only immediately after treatment, and by Litt & Porto (2013). One problem with these studies is that changes in general orientations toward pain that appeared posttreatment may have been the result of symptom improvement rather than the result of specific practices or skills learned in CBT. It is also not clear whether more active control conditions might not have also shown such improvements in adaptive cognitions.

In addition to specific cognitions, mood states, too, should be altered by effective coping (Turk et al., 1996). Negative moods will set the stage for momentary pain, and contribute to pain several hours later. Our data indicate that pain then leads to subsequent negative mood (Litt et al., 2009), in a dynamic process. But few treatments have documented improved mood as a result of treatment. Finally, not all cognitive-behavioral treatments have performed as well as that of Turner et al. (2007)(see, e.g., Aggarwal et al., (2010)). In their review and meta-analysis Morley et al. (1999) concluded that CBT did not always yield improvements in several domains that are typically targeted, including mood, cognitive coping, and negative appraisals such as catastrophization, *suggesting a need for treatments that more effectively train coping skills, or else, a*

reevaluation of the social learning model of pain management. Similar findings were reported by Iwasaki et al. (2018). The specific personalization of treatment, through precise assessment of skills, cognitions and moods as they occur before, during, and after pain episodes, will address these issues and target those skills that need training. Other mechanisms may also play a role, and should be addressed by treatment.

Alteration of bruxing. Glaros (2008) among others noted the significant contribution of parafunctional activities, particularly clenching and nocturnal bruxing, to the development and maintenance of TMD pain. It has been suspected that certain interventions, particularly the use of a splint (Harada et al., 2006; Klasser et al., 2010) and the teaching of relaxation and stress management skills may reduce bruxing and thereby reduce TMD pain (Ommerborn et al., 2007). These ideas have never been clearly tested, however, and it is not clear how much variance in everyday pain is accounted for by parafunctional habits, or how many patients are affected. Psychological flexibility: Acceptance and Commitment. The last several years has seen the advent of a somewhat new approach to psychosocial pain treatment, called the psychological flexibility (PF) model (e.g., McCracken & Morley, 2014). This approach has many of the hallmarks of (sophisticated) cognitive-behavioral treatment, including objective observation and analysis of thoughts and feelings (especially catastrophizing), but also entails an attitude toward negative moods and cognitions that is characterized as new. The attitudes of acceptance and commitment (ACT) emphasized in this approach suggest that patients should “accept” a certain degree of pain and act despite the pain (commitment), if such actions are consistent with their values (e.g., determination to live life despite pain). Additionally, certain thoughts and feelings about pain, which would trigger distraction or other strategies in CBT, would in the PF model be passively accepted and experienced. This approach, articulated by Hayes (Hayes et al., 1999), asserts that the goal should be to extinguish the associations between pain and maladaptive thoughts by not attending to them. The passive acceptance of these thoughts is enabled by practices like mindfulness meditation (Segal et al., 2002; Teasdale et al., 2000). Some evidence indicating that these approaches do mediate outcomes has been forthcoming (Vowles et al., 2014) but never in a well-controlled trial.

“Common Factors”. Somewhat contrary to the idea that specific aspects of treatment (e.g., skills training) are responsible for adaptive change, the common factors model suggests that less specific aspects of the treatment experience are responsible for producing treatment-related changes. These common factors include: (especially) the therapeutic alliance; interpretation and understanding; emotional expression; reinforcement; information; reassurance and support; expectancies; time; and the placebo response (Garfield, 1995; Imel & Wampold, 2008). Although the common factors are undoubtedly important, it is not clear how they translate into initial or prolonged behavior change or adaptation. This, too, is a subject for research, and will be measured here.

What’s Going On? Retrospective Reports

One significant problem in our understanding of mechanisms of action of treatment is that information tends to be gathered retrospectively. This is particularly true of coping and of self-efficacy. Self-efficacy was intended to be a measure of a person’s confidence at a given moment in time. Currently, self-efficacy is often measured generally, and may thus be reflecting dispositional optimism more than true self-efficacy. A measure of self-efficacy that occurs more proximal in time to the event (pain) of interest is needed. Coping behaviors represent another problem for measurement. Although patients may report using certain strategies, the reports may not be accurate (Ptacek et al., 1994; Todd et al., 2004). Retrospective reports are essentially narratives, influenced by the person’s need to explain his or her actions, or to simply make coherent a set of poorly connected memories (Mandler & Johnson, 1977). In addition, recollections of events are often dominated by the atypical or dramatic (Mandler & Johnson, 1977; Reiser et al., 1985), and are influenced by both intervening events and contemporary moods and cognitions (e.g., Loftus, 1979). This problem may partly account for the often low predictive power of coping strategies in explaining treatment outcomes (e.g., Tota-Faucette et al., 1993).

Current measures may represent central tendencies rather than actual behavior. *To accurately assess cognitions, affects and behaviors at critical periods in a pain patient’s day requires an assessment paradigm that allows the patient to record almost at the time events occur, and which do not allow time for reflection or processing.* We propose such an assessment procedure here.

Experience Sampling in Pain Patients

A growing number of studies demonstrate that chronic pain patients are quite amenable to recording pain and pain-related situations daily or multiple times per day (e.g., Stone et al., 2005; Tennen et al., 2006). Stone et al. have documented that such measurements tend to be more accurate (predictive) than retrospective measurements, which are affected by the variability of day-to-day pain experiences. In our own studies (summarized below) TMD patients have recorded 4-8 times per day, with an adherence rate of 70% or better. In addition, momentary measurement of coping per se is more likely to capture certain responses, such as cognitive coping actions, as well as *absence* of adaptive coping, than retrospective measurement schemes (Litt et al., 2009; Stone et al., 1998).

Moderators of Treatment

Whereas coping, catastrophizing, self-efficacy and positive-negative affect are presumed to mediate treatment effects, other, dispositional, variables are likely to help determine who responds best to what type of treatment. In the TMD literature, Turk et al. (1996) provided evidence that patients who report emotional and physical difficulties would benefit more from a treatment that included cognitive therapy than from a comparison treatment that did not. Litt et al. (2010), evaluated moderators of treatment for TMD patients assigned to standard conservative treatment or standard treatment plus CBT. Those who fared best with CBT tended to be those who were least severe and could best make use of the cognitive elements of treatment. Those high in somatization, for example, actually tended to fare better with standard treatment. It is possible that the highly involving CBT actually prompted somatizers to attend more to their pain problem. This possibility can be tested by assessing somatization in-vivo. Readiness for treatment and self-efficacy were also moderators of treatment effects, and will be measured here. We believe a tailored coping skills program can improve outcomes for those who are high in somatization or catastrophization.

Purpose and Significance

The purpose of the present study is twofold: First, to devise a treatment that more effectively assesses patient needs and addresses those needs specifically. The experience sampling procedure in the IATP component will provide very accurate assessments of cognitions, affects and behaviors at critical periods in a pain patient's day. Such an assessment of situation-specific coping and cognitions will be used by a therapist to determine what a patient is doing well or doing poorly in the face of a painful episode or stressor. The momentary assessment process would thus provide the basis for highly tailored coping skills-based treatment specific to the patient's strengths, weaknesses, and specific situations. We believe this will result in more effective treatment. Second, to determine how psychosocial treatments effect their outcomes in a chronic pain population. To do this we intend to examine situation-specific cognitive, affective and coping factors through the course of treatment, and determine which are driving changes in pain/adaptation, even into the long-term. A highly tailored treatment like that described, matched against an effective but non-tailored treatment that controls for time and attention, **would be significant both theoretically and clinically.**

If individualized coping skills and adaptive cognitions are important determinants of outcome for pain patients, then the IATP should prove to be an especially effective treatment approach, applicable not only to TMD patients, but to a number of pain populations that have similar characteristics.

The study will also provide a strict test of the cognitive social learning model of treatment for chronic pain. By providing an optimal coping-skills based treatment, and measuring use of those skills during and after treatment, we will be able to test the influence of these constructs in determining outcome.

C. INNOVATION

Use of Experience Sampling (ES) to measure coping and drive treatment. In the proposed study experience sampling procedures will be used to measure pain, coping, moods and cognitions multiple times per day. In this way we will capture both pain episodes and non-pain episodes. Thus we will have non-pain records that will be used to control for records in which pain is recorded, allowing true testing of the role of momentary variables on pain and its aftermath. The use of these data to tailor treatment to specific patient strengths, weaknesses, and situational constraints is highly innovative, and has the potential to make treatment highly effective.

Treatment is adaptive. By adding experience sampling periods during treatment, we will get a look at the changes that take place in coping and cognitions as a function of treatment, and therapists will be able to use

the information collected to *adapt treatment* to changing patient skills and needs as treatment proceeds. Repeated experience sampling periods posttreatment and during the follow-up periods will allow us to detect the degree to which patients continue to adapt and cope, even well after treatment ceases. The ability to detect changes during and after treatment is also innovative.

Examination of mechanisms of action in psychosocial pain treatment. As noted above, studies of mechanisms of action of psychosocial treatments for chronic TMD pain have been relatively rare. In studies with pain patients, both the active coping strategy (e.g., Litt et al., 2009) and the acceptance strategy (Vowles et al., 2007) have chalked up successes. A likely possibility is that some people respond better to a more control-oriented approach, and some better to acceptance. This study of active mechanisms and specific moderators will help to answer this question.

Use of an effective foundation & control treatment (STD+CBT)

In our previous studies and in clinical practice, conservative treatment that incorporates the use of a flat-plane splint has demonstrated a high degree of efficacy. The addition of CBT to standard treatment will provide a stringent control for IATP. STD+CBT has proven efficacious (Litt, Shafer, & Kreutzer, 2010), delivering coping skills training but without the individualization of IATP. Having an active foundation treatment (rather than treatment as usual) is somewhat uncommon in this field, and will allow us to determine the added value of individualized treatment, while assessing the mechanisms by which patients improve and controlling for common factors.

Preliminary Studies

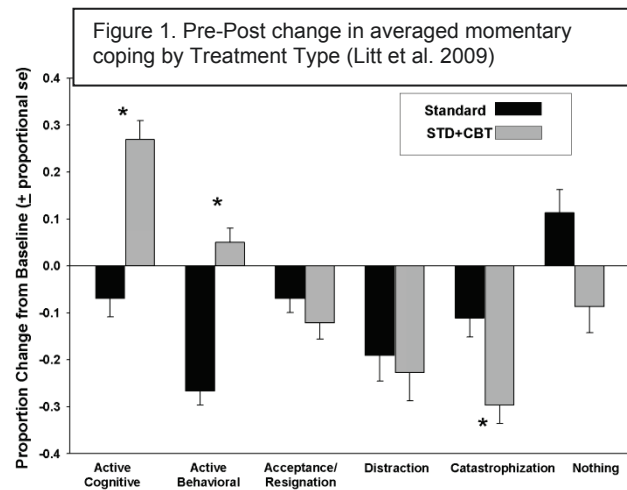
Coping with TMD

For 10 years we collected basic data on TMD patients referred to the Oral and Maxillofacial Surgery Clinic at the UConn School of Dental Medicine. In one study we sought to explore the effects of causal explanations on coping strategies used, depression, perceived pain control and total pain in persons presenting with complaints of TMD pain (Litt & Kalinowski, 1997). Causal explanations fell into five categories based on occurrence of trauma and locus of responsibility. Active coping was most used by those who attributed their pain problem to stress or emotional upset ($p < .05$). Dispositional factors (in this case attributional style) interacted with situational factors (coping strategies) to determine level of distress in the context of an enduring stressor, TMD.

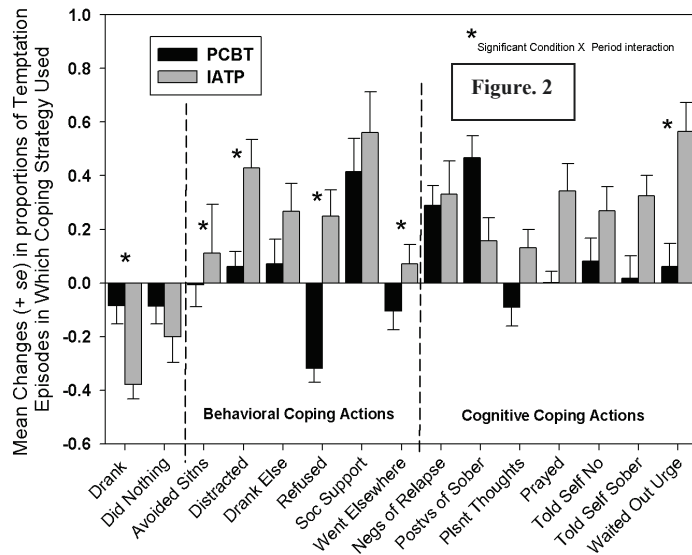
Brief Treatment and ES in TMD Patients

In a pilot study of treatment (Litt, Shafer, & Napolitano, 2004) patients with TMD pain of at least 6 months duration (N=30) were issued handheld computers that prompted them to record their momentary pain and coping processes 4 times per day for 7 days. Hierarchical linear regression models indicated that momentary pain was a function both of dispositional tendency to catastrophize and of momentary measures of catastrophization, self-efficacy, and mood states. This study provided support for the causal role of catastrophizing. Lagged analyses indicated that although catastrophizing contributed to pain experience a few hours in the future, the reverse was not true. Higher pain did not lead to greater

catastrophizing. It was concluded that catastrophizing will need to be a focus of treatment, given its significant role in pain episodes. In a subsequent full-scale treatment study by Litt et al. (2010), 101 TMD patients were assigned either to a standard conservative treatment (STD) or standard treatment plus CBT (STD+CBT). The addition of CBT to standard treatment resulted in significant long-term gains in pain and depression symptoms (at 18 mo; Litt, Shafer, & Williams, March 2003). Interestingly those who fared poorly with the addition of CBT were those who were least well adapted to start (lower in self-efficacy and readiness, higher in somatization)(Litt & Porto, 2013). It was concluded that for CBT to be optimally effective it needs to develop greater focus on the specific vulnerabilities of patients, providing support for a more individualized approach.



Experience sampling data indicated that, at posttreatment, the STD+CBT patients reported less momentary pain than the STD patients, and greater increases in momentary coping and less catastrophizing (Litt et al., 2009). Posttreatment momentary pain was negatively predicted by concurrent active coping, self-efficacy, perceived control over pain, and positive-high arousal mood. Concurrent catastrophization was strongly predictive of pain. Active behavioral coping and self-efficacy reported at the prior time point (about 3 h previously) were also protective, while prior catastrophization and negative-high arousal mood were predictive of momentary pain. The results suggested that CB treatment for TMD pain can help patients alter their coping behaviors, and that these changes translate into improved outcomes. It is expected that more focused CBT would enhance outcomes.



IATP in Alcohol Dependent Patients. We have experience developing the momentary-assessment-based treatment proposed here (Litt, Kadden, & Kabela-Cormier, 2009). 110 men and women were assigned randomly to a comprehensive packaged CBT program (PCBT), or to an Individualized Assessment and Treatment Program (IATP), each 12 weeks in duration. The IATP program employed experience sampling 8 times per day via cellphone to assess coping skills prior to treatment, and provided therapists a detailed understanding of patients' coping strengths and deficits. IATP yielded higher proportion days abstinent (PDA) at post-treatment than PCBT. IATP patients reported significantly fewer temptation episodes at posttreatment than did the PCBT patients. IATP also elicited more momentary coping responses, and less drinking, in high risk situations, as recorded by experience sampling (see Figure 2). The IATP approach was more successful than PCBT at training adaptive coping responses for use in situations presenting high-risk for drinking. The process of using real-time data to train patients in coping is feasible and has potential.

APPROACH

The basic design and procedures of the study are shown in Figure 3. We propose a two-group repeated measures design in which patients presenting with TMD pain are assigned to either a Standard Treatment plus Programmed Cognitive-Behavioral Treatment (PCBT), or to a condition in which a standard treatment is augmented with the cognitive behavioral IATP treatment that focuses on tailoring training to the needs of the patient, based on real-world instances of confronting painful stressors. Patients will be followed at 3mo intervals to monitor fluctuations in pain and coping over time, and to help insure that patients remain engaged.

Method

SUBJECTS

Recruitment. Subjects (N=160) will be recruited from the Hartford metropolitan area through periodic radio and newspaper advertisements, as well as web-based advertising, offering free short-term treatment for TMD, and via referrals from clinical services at the UConn Health Center. We have successfully recruited an average of 5 subjects per month. With this rate of recruitment we will recruit our needed N in 36 months.

Inclusion/exclusion and recruitment rate. Subjects will be healthy male and female volunteers, aged 18 years or older, seeking treatment for a complaint of either bilateral or unilateral pain roughly in the area of the temporomandibular joint that has persisted for a period of at least 3 months, and scoring at least 3 on a 0-10 pain scale. Inclusion and exclusion criteria are shown in Table 1.

Power analysis. Sample size was determined by ability to evaluate the primary aim of this project. Sufficient subjects will be recruited to detect between-group differences over follow-up on the primary outcome variable, pain intensity. Sample size determination was conducted using the PASS 16 (2018) software package, using the procedure for estimating power from a hierarchical mixed model longitudinal design with fixed slopes, based on work by Ahn et al. (2015). The effect size estimate for pain and the autocorrelation of reports were

based on our earlier treatment study, and represent conservative estimates. The difference in slopes for pain in the proposed study is estimated at .12 (SD=.30). The number of (unequally spaced) time points is 6 (baseline, posttreatment +4 follow-ups). The within-subjects correlation (autocorrelation) is estimated at $\rho=.54$. Given a power of .80, alpha set at .05, and equal numbers of subjects per condition, the required N would be 130 ($n=65$ per condition). Power for mediation: Power for mediation was determined using the online application “MedPower” (Kenny, 2017) , based on path coefficients from earlier work (Litt & Porto, 2013) for coping change. Given $a\text{-path}=.24$; $b\text{-path}=-.48$, and $c' \text{ path}=-.61$; an N of 133 would be sufficient for to detect a significant partial mediation effect with $\text{power}=.80$. Therefore, in order to detect the primary treatment and mediation effects, we would require 133 subjects. Anticipating ~20% attrition at 1 year, we will recruit 160 patients (80 per condition). We currently see ~10 patients/mo who would meet eligibility. We should have no difficult recruiting 4-5/mo over 36 mo for this study.

Inclusion of women and minorities. In our earlier work 84% of our sample was female, a proportion that is representative of the condition’s prevalence in the treatment-seeking population. In addition, 9% of the sample was Hispanic and 9% African-American. Outreach to Hartford area clinics (e.g., Hispanic health council) will also be done, however, to further encourage minority enrollment, as well as men.

Table 1. Patient Inclusion/Exclusion Criteria	
Inclusion Criteria	Exclusion criteria
1. Age ≥ 18 years 2. Jaw pain ≥ 3 mo; $\geq 3/10$ on pain scale 3. Positive Axis I diagnosis on the Diagnostic Criteria for temporomandibular disorders (DC/TMD), with or without disc displacement; Positive on ≥ 1 of: <ul style="list-style-type: none"> • Any myalgia diagnosis • Any myofascial diagnosis • Arthralgia • TMD-related Headache 	1. Lack of fluency in English 2. Previous surgery for TMD 3. Extensive anatomical destruction or deterioration of the TM joint 4. Diagnosed as having pain of neuropathic or odontogenic origin 5. Carrying a diagnosis of psychosis 6. Current treatment for depression 7. Taking narcotic pain medication 8. Any comorbid condition necessitating use of an intraoral appliance (e.g., obstructive sleep apnea) 9. Pregnancy (excluded due to prescription of NSAIDs)

MEASURES AND INSTRUMENTS (Most instruments will be administered online, via REDCap)

Screening and Classification (SCID & DC/TMD Axes I and II)

Initial screening of potential subjects will be conducted over the telephone using an inclusion/exclusion criteria checklist administered by a research associate. In-person screening will be conducted using the psychotic screening portion of the Structured Clinical Interview for DSM-V (SCID V; First et al., 2015), plus the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure—Adult (APA, 2013), which can screen for a variety of psychiatric issues, including depression, suicidal ideation, anxiety, and sleep disturbances, among others. Classification of TMD subjects’ orofacial pain problem will be done using the revised Diagnostic Criteria for Temporomandibular Disorders History Questionnaires (Ohrbach R. (Editor), Version 15May2016; Schiffman et al., 2014). The DC/TMD procedures are an update of procedures laid out by Dworkin & LeResche (1992), with increased sensitivity and reliability of diagnoses, particularly in Axis I. The examination will be conducted by our oral surgeon and orofacial pain specialist investigators, who have experience with the DC/TMD examination. Prior to patient recruitment the examiners will train on sample cases using the DC/TMD procedures manual until they attain 90% interrater agreement on specific Axis I diagnoses. During the recruitment phase the examiners will test on each 20th case to maintain reliability. DC/TMD Axis II assessment will be conducted using the following, as per the assessment manual: The Jaw Function Limitation Scale (JFLS-20; Ohrbach, Granger, List, & Dworkin, 2008); The Patient Health Questionnaire (PHQ-15; Kroenke, Spitzer, & Williams, 2002); The General Anxiety Disorders scale (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006); and the Oral Behaviors Checklist (Ohrbach, Markiewicz, & McCall, 2008).

Dependent Variables (IMMPACT recommendations)

The primary dependent variables in this study will be **Pain Intensity, Depression and Interference**. A number of secondary outcomes will also be assessed and analyzed as per guidelines from the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT; Haythornthwaite, 2010; Turk et al., 2003). All outcomes will be evaluated on day of recruitment (baseline) and again at the follow-up points [7 weeks (posttreatment), 3 months, 6 months, 9 months, and 12 months]. The six outcome domains are: (1) pain

(including intensity and pain experience); (2) physical functioning; (3) emotional functioning; (4) participant ratings of improvement and satisfaction with treatment; (5) symptoms and adverse events; and (6) participant disposition (e.g. adherence to treatment, reasons for premature withdrawal). Specific instruments were chosen on the basis of recommendations by Haythornthwaite (2010). Several instruments were included because they have proven useful in our previous studies, and may form a basis for comparison. All instruments chosen have demonstrated acceptable psychometric characteristics.

Pain intensity at each assessment point will be calculated as Characteristic Pain Intensity by averaging ratings of current pain, average pain, and worst pain in the past week from the Graded Chronic Pain Scale (GCPS; Von Korff et al., 1992); a reliable retrospective measure (Stone et al., 1997). Each item is scored from 0 -10. Other dimensions of pain per se, (sensory and affective dimensions), will be assessed using the short form of the McGill Pain Questionnaire (MPQ-SF; Melzack, 1987).

Physical functioning. General interference with activities will be measured using the interference scale from the Multidimensional Pain Inventory (MPI; Kerns, Turk, & Rudy, 1985). The MPI also contains questions about sleep, which is often affected in pain patients. Jaw function will be assessed using the Jaw Functional Limitation Scale (JFLS; Ohrbach et al., 2008). The JFLS is a 20-item questionnaire that assesses mastication, jaw mobility, and verbal and emotional communication.

Emotional functioning. Depression symptoms will be measured using the using the 20-item Center for Epidemiological Studies Depression scale Revised (CESD-R; Eaton et al., 2004), a useful measure of distress in medical populations. In addition we will measure anxiety mood using the Trait version of the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1983).

Participant rating of improvement will be assessed with the Patient Global Impression of Change scale (PGIC; Hurst & Bolton, 2004). The PGIC consists of two questions in two different formats asking for a global assessment of “change if any, in activity limitations, symptoms, emotions and overall quality of life.” A 2-point change on the rating scale has been calculated to be clinically significant.

Symptoms and adverse events will be collected weekly during treatment by therapists, and by research assistants at each follow-up. Procedures are described in the Human Subjects section.

Participant disposition, including retention in treatment and follow-ups, and reasons for withdrawing, will be collected in a patient tracking database.

Dispositional Variables-Moderators/Mediators

A number of instruments will be administered at intake into the study, and explored in secondary analyses for their role as potential *dispositional* moderators based on past research. General perceptions of coping will be assessed using the Brief Pain Coping Inventory (BCPI; McCracken et al., 2005). The Pain Catastrophizing Scale (PCS; Sullivan et al., 1995) will be used to assess catastrophizing . The Chronic Pain Acceptance Questionnaire (CPAQ; McCracken et al., 2004) will also be used to assess Acceptance approaches to pain (Activity engagement; Pain willingness). Generalized pain self-efficacy will be measured using the Facial Pain Self-Efficacy Scale (Brister, Turner, Aaron, & Mancl, 2006). The Social Support for Pain Coping questionnaire is based on the spouse support factor of the MPI. Somatization will be measured using a subscale of the Patient Health Questionnaire, the PHQ-15 (Kroenke et al., 2002) administered as part of the DC/TMD protocol. The PHQ-15 has been validated as a useful measure of somatization (Kocalevent et al., 2013). Neuroticism will be tapped with the 12-item NEO neuroticism scale (Costa & McCrae, 1992). Readiness to engage in self-management treatment for chronic pain will be assessed using the Pain Stages of Change Questionnaire (Kerns et al., 1997). Common factors : It has been suggested that the effectiveness of therapy is ultimately attributable to the therapeutic relationship (e.g., Barber et al., 2000), and other factors common to therapy (see Imel & Wampold, 2008). This possibility will be assessed with the Working Alliance Inventory (WAI; Horvath & Greenberg, 1986) client version short form (Tracey & Kokotovic, 1989).

Figure 3. Design and Timeline of procedures

Treatment Condition	Session/Time Point										
	Baseline Wk -1, 0	Wk 1	Wk2	Treatment Wk 4 Wk 5 Wk 6			Wk 6-7	Follow-up 3 Mo 6 & 9 Mo 12 Mo			
Standard Treatment +CBT (STD+CBT) STD+IATP	Screening										
	Pan X-Ray										
	RDC Exam										
	Baseline Measures							Post-Tx Measures	Follow-up Measures	Follow-up Measures	Follow-up Measures
	Treatment Assignment	Splint Delivered			Splint Taper - night only	Splint Discont'd					
	Impressions for splint	STD + CBT Patients Session 1	STD + CBT Patients Session 2		STD + CBT Patients Session 4	STD + CBT Patients Session 5	STD + CBT Patients Session 6				
		IATP Patients Session 1	IATP Patients Session 2		IATP Patients Session 4	IATP Patients Session 5	IATP Patients Session 6				
4 Times Daily Monitoring (14 Days)	Start NSAIDs	Taper NSAIDs					4 Times Daily Monitoring (7 days)	4 Times Daily Monitoring (7 days)		4 Times Daily Monitoring (7 days)	

Experience Sampling (ES) of pain, coping, and affects via Smartphone app

The use of Experience Sampling (ES) in both the STD+CBT and STD+IATP treatment conditions allows us to assess use of coping skills, while avoiding many of the problems inherent in retrospective recording (Stone & Shiffman, 2002). Experience sampling will be conducted through the use of a smartphone app, in which assessments are made when participants are prompted by the phone and connect to a proprietary link to a series of questions. During the training session participants will be instructed to answer each question with as little reflection as possible. Participants will be asked to carry their phone at all times in Weeks -1 and 0 (after baseline interviews, but before treatment starts), for 7 days during weeks 2 & 4 while in treatment, and again for 14 days after completion of treatment, and later during follow-ups (see Figure 3). The smartphone-based ES system, known as PiLR (MEI Research, LTD), will administer surveys, and record responses.

The system will be programmed to prompt subjects on a quasi-random basis 4 times per day, with one randomly scheduled prompt in each of four 210-minute time periods from 8:00AM to 10:00PM (adjustable for different schedules). This frequency of recording was chosen to enable us to capture as many moments in a patient's day as possible without being disruptive (Litt et al., 2004; 2010). Subjects will have the option of delaying responding to a prompt for 5, 10 or 15 minutes if recording is inconvenient.

ES Recording format. Participants will respond to survey questions on the phone screen. For every recording the subject is directed to record perceptions along a 7-point "slide-scale" ranging from "0=Not at all" to "6=Very much." Responses are time-and-date-stamped, and entry of out-of-range data is not possible. If data entry is abandoned in the midst of an assessment, the system will prompt the participant again and resume the assessment. Assessment data will be electronically stored in spreadsheet format on a system server maintained by MEI Research, backed up nightly, and accessible in real time. Data from each participant engaged in ES monitoring will be examined each day for missing responses by a research assistant. If a participant misses two recordings in a row, the research assistant will contact the individual by phone or text. Compliance rates for experience sampling in our last study were: at pretreatment 72% of calls were completed; at posttreatment 71% of calls were completed.

ES data. Patients will respond during ES to items related to pain intensity (right and left sides of the face) and unpleasantness experienced (right and left sides), and two items related to perceived control over pain ("am able to decrease pain;" "am able to control pain"). Self-efficacy will be measured with: "How confident are you that you can cope with your current pain?" Catastrophization will be assessed using two items borrowed and modified from the Coping Strategies Questionnaire (CSQ; Rosenstiel & Keefe, 1983) catastrophization subscale, are "Worried about Pain" and "Pain is Terrible," ($\alpha = .87$). Somatizing will be measured using 2 items reflecting the tendency to process stress in terms of physical symptoms: "Concerned that jaw will start hurting," "Paying attention to my jaw pain."

Current mood state will be recorded using 8 items derived from a semantic space analysis of adjectives in the circumplex model of affective experience (Larsen & Diener, 1992; Russell, 1980). The items are combined to

yield four reliable mood composites based on dimensions of pleasantness and arousal (internal reliability alphas exceeded 0.80 for all four affect subscales in previous samples).

Situations will be assessed using categories (Home, With others, etc.), as well as with free voice response.

Coping responses will be recorded by asking the subject what if anything he or she had done to help manage any pain he/she might have experienced in the last 10 minutes. The 12 coping response items were derived from inventories assessing coping in pain patients (e.g., the CSQ), and from surveys of patients in TMD pain treatment, and grouped into 4 subscales: active-behavioral (e.g., “I used ice or heat,” “Relaxed”); active-cognitive (e.g., “I thought pleasant thoughts”); resignation (“I just accepted the pain”); and distraction (“I distracted myself,” “I looked for support from someone”). One item also recorded if “Nothing” was done to deal with the pain. Internal consistency reliabilities of the coping subscales exceeded $\alpha=.65$ in past studies. Two items will be added reflecting Acceptance-based strategies (as opposed to pain control–related strategies; Hayes et al., 1999) based on Vowles et al.(2007): “Tried to accept the pain and focus on what I was doing; “Told, myself that the pain does not have to stop me.” An additional item reflects “guarding,” which is characteristic of somatizing, “Restrict my activity to keep from hurting myself.” Patients will also be asked to record an answer using free response (voice recording), to be categorized by the RA staff later. This will allow us to compare free responses with categorized ones. Consequences of the response will also be assessed.

Therapists’ data summary. Prior to the beginning of treatment, all of the responses collected in ES will be collated by the research assistants and provided to the therapists for use in the STD+IATP condition, and will form the basis for Functional Analysis (see Figure 4). Data regarding situations associated with pain, affects, cognitions, and coping actions will be used to devise specific adaptive coping responses to pain episodes. The same procedure will be used during treatment, at weeks 2 & 4, to modify and adapt treatment. That is, ES data from weeks 2 & 4 will be summarized and presented to the IATP therapist. The data will be examined for new situations that present problems for the patient, and that call for development of new coping strategies. In this way the treatment will be adaptive, changing with the needs of the patient.

Reactivity of ES. One concern is the possible reactivity of the ES procedure, the possibility that frequent prompts may alter reporting, or sensitize patients to pain. Reactive effects, should they occur, will not threaten the internal validity of the study because all subjects (STD+CBT, STD+IATP) will participate in the same ES protocol. However, research to date suggests that sensitization or reactivity to momentary monitoring in pain patients has not been found (Aaron et al., 2005; Stone et al., 2003).

TREATMENT

**Manuals for both of the treatments described here have already been developed.

Both Treatments will consist of Standard Conservative Treatment (described) plus a psychosocial component over 6 weekly sessions. **Patients in both treatment conditions will have 10 weeks in which to complete the 6 sessions.**

Standard Conservative Treatment

Standard Treatment (STD) will consist of splint therapy plus soft diet and oral anti-inflammatory agents (Canales et al., 2016; Stack & Stack, 1992). The primary rationale for this aspect of treatment is to change the oral habits of patients with respect to clenching and bruxing, and to provide a sufficient respite from pain to allow more adaptive oral habits to emerge (despite the admitted lack of evidence for these processes). Splint delivery, soft diet recommendations, and supplying of NSAIDs will **all occur on the first treatment day**, and take place in the dental CRC.

Maxillary Splint: As noted below, impressions will be taken for the fabrication of an acrylic flat-plane maxillary splint during the Diagnostic Evaluation (DE) for those person who are eligible for treatment. Patients will receive the intraoral splint during the first treatment visit, 2 weeks after the DE visit. A dental assistant will deliver the splint. One of the investigator-DMDs will be on hand to adjust the splint for comfort and fit if necessary. Patients will be given instructions to keep the splint in place continuously (except for eating) if possible for the succeeding 4 weeks. If this proves too difficult patients may elect to use it only at night. After 4 weeks it will be recommended to patients that they start to taper the splint (e.g., use only as a night guard) in preparation for discontinuing the splint altogether. The purpose of this is to try to prevent the patient from becoming so comfortable with the splint that he/she starts clenching or bruxing on the splint itself. However, we discovered in our earlier work that many patients (~50%) elected to retain the splint and to wear it especially as a night guard, with good results, whereas others discontinued the splint as recommended (also with good

results). Given the good outcomes found regardless of duration of use of the splint, we will make the recommendation for discontinuation, but not require patients to stop using the splint if they feel it is useful for them. Splint use will be monitored throughout the course of the study, and amount of use will serve as a variable for later analysis.

Instrument	Intake In- Person, DE	6 wks (Post-Tx) In-Person	3-mo. In- Person	6-mo In- Person	9-mo. In- Person	12-mo. In- Person
SCREENING & Dx Eval VARIABLES						
Quick Screen, Demographics	X					
Slosson Oral Reading Test (if indicated)	X					
SCID V: Psychotic Screen	X					
DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure	X					
DC-TMD Examination	X					
DC-TMD Pain locations drawing	X					
Jaw Functional Limitation Scale-long form (JFLS)	X					
Generalized Anxiety Disorder-7 (GAD-7)	X					
Physical symptoms Patient Health Questionnaire-4 (PHQ-4)	X					
Physical symptoms Patient Health Questionnaire-9 (PHQ-9)	X					
Physical symptoms Patient Health Questionnaire-15 (PHQ-15)	X					
Parafunctional Oral Behaviors Checklist (OBC)	X					
Client locator form	X					
DEPENDENT MEASURES						
Graded Chronic Pain Scale	X	X	X	X	X	X
Jaw Functional Limitation Scale-Short form (JFLS)	X	X	X	X	X	X
MPI - Interference	X	X	X	X	X	X
CES-D	X	X	X	X	X	X
STAI-Trait	X	X	X	X	X	X
Pt Global Impression of Change	X	X	X	X	X	X
PROCESS VARIABLES						
Brief Pain Coping Inventory	X	X	X	X	X	X
Pain Catastrophizing Scale	X	X	X	X	X	X
Chronic Pain Acceptance Questionnaire	X		X	X	X	X
Facial Pain Self-Efficacy Scale	X	X	X	X	X	X
MPI – Spouse support	X		X	X	X	X
PHQ15 somatization	X		X	X	X	X
NEO neuroticism	X		X	X	X	X
Pain Stages of Change Quest			X	X	X	X
Working Alliance Inventory (WAI-C-Short Form)*	X					
Experience Sampling Measures‡	X	X	X	X	X	X

* The WAI will be administered to participants and therapists after the 2nd treatment session.
 ‡Experience Sampling via smartphone app Process measures will be taken 4 times per day for 2 wks, between Intake & treatment start (Weeks -2 to 0), and at **Wks 2 and 4 (during treatment), 6 (posttreatment), 12, and 48**

Non-steroidal anti-inflammatory medication: In addition to the splint, subjects will be placed on a 14-day course of non-steroidal anti-inflammatory medication (NSAIDs; naproxen sodium 550 mg po BID; or 600 mg ibuprofen TID or QID). Extra strength Tylenol (500 mg) will be substituted for naproxen for those patients who claim to have difficulty with NSAIDs or who have gastric ulcer disease. One of the attending oral surgeon-investigators will prescribe the medication at the time of the DE, based on patient history and report. The prescription will be filled by the UConn Health Pharmacy, and the 14-day supply of the appropriate medication will be delivered to the Dental CRC for delivery to the patient by the dental assistant on Day 1 of treatment, at the same time as the splint delivery.

Soft Diet: A soft diet will also be prescribed with special attention paid to avoiding foods that require extreme jaw opening (e.g., large sandwiches) or foods that have caused pain in the past (e.g., steak). Patients will be given a brochure explaining an appropriate diet.

Patients will be asked to continue using the splint and the soft diet until the end of the 6-week treatment period, after which they will be informed that they may alter the treatment as they see fit (e.g., discontinuing the splint), but recommending care in their diet.

Cognitive-Behavioral Treatment (CBT)

Session	Topic
Session 1.	Introduction, Rationale & Establishment of Rapport. Patients given common-sense explanation of multidimensional nature of pain; relate TMD pain to stress and to habits; emphasize importance of relaxation and adaptive coping. Pain monitoring
Session 2.	Relaxation with Mindfulness, Self-Efficacy Enhancement. Recap of importance of relaxation as coping. EMG biofeedback assisted relaxation of masseters, along with mindfulness meditation. Verbal feedback re: good progress. Home relaxation.
Session 3.	Habit Modification. Discussion of role of parafunctional habits in TMD, including bruxing, clenching; discussion of using awareness, alternative behaviors to break habits. Homework: Self-monitoring of parafunctional habits, with notes on ways to decrease these.
Session 4.	Combating Negative Thoughts and Catastrophizing. Discuss importance of negative moods and thoughts, especially catastrophizing, discuss alternatives. Homework: Self-monitor pain and responses, while noting alternative adaptive coping actions.
Session 5.	Stress Management: Coping in Action. Review all aspects previously covered. Examine how topics covered with respect to TMD also apply to other areas of life (e.g., work performance, social anxieties). Generalize progress in working on TMD to raise self-efficacy for managing stressors in general.
Session 6.	Overview & Recap Reemphasize improved ability to manage TMD (enhance self-efficacy), discuss again patients' efforts to stop catastrophization re: TMD; encourage application of techniques to other stressors.

The CB treatment (CBT) will consist of 6 sessions focusing on the development of skills thought to be necessary for the self-management of chronic TMD pain. These include relaxation training, stress management, and cognitive restructuring intended to promote self-efficacy and to reduce catastrophization. The cognitive-behavioral program is based on a brief program developed by Turk et al. (1993), and modified for our earlier treatment study (Litt et al., 2009; 2010). The therapy will consist of 6 one-hour sessions over 6 successive weeks. The CBT program is intended to teach skills to keep the patient from returning to old habits and clenching, bruxing, and catastrophizing cognitions that contribute to TMD pain and distress. As with our earlier trial the therapy will be manual-driven, giving the therapists specific guidelines as to what material to cover, what points to emphasize, and the specific kinds of homework to be assigned. The precise content of therapy sessions will depend on the individual patient's circumstances and experiences. (For example, all patients will be given assignments to practice relaxation. The circumstances in which they do this, however, will be determined by the patients.) An session-by-session outline of the focused CBT appears in Table 3.

Individualized Assessment and Treatment Program (STD+IATP)

Basic outline: The 6-week STD+IATP treatment will include all aspects of the STD treatment described above. In addition, patients will receive IATP, a brief, highly individualized, cognitive-behavioral program that may include relaxation training, stress management, and cognitive restructuring. The basic outline of the IATP sessions is based on a brief program developed by our group in earlier work (See Table 4). The extent to which any particular skill is focused upon will be determined by the Functional Analysis derived from the ES data. Some topics may be dropped altogether if the Functional Analysis indicates that the patient already has that skill (e.g., relaxation), or if some approach is clearly not effective (e.g., habit modification), whereas other topics may occupy multiple treatment sessions (e.g., managing catastrophizing). Unlike CBT, IATP is designed to focus on patients' coping with specific pain episodes in near real time, rather than on more general assessments. Data regarding pain episodes and their associated affects, cognitions, and coping actions will be used by the therapist and client together to problem-solve and devise adaptive coping responses to these specific high-risk situations. The same procedure will be used at Weeks 2 and 4 during treatment, to modify and adapt treatment. At these later visits new challenges will be apparent from the ES monitoring, and different skills will be discussed. Although functional analysis and altering treatment are supposedly features of all CBT programs, assessment is typically general and retrospective. In contrast, the ES described here allows recording of thoughts, feelings and behaviors close to the time they occur. Therapists will initially focus on situations in which most pain occurs (high risk), and subsequently will attend to the patient's changing needs as indicated by the during-treatment ES records (in Weeks 2 and 4) adjusting the treatment plan as needed. As with our earlier studies the therapy will be manual-driven, giving the therapists specific guidelines as to how to cover specific skills, what material to cover, what points to emphasize, and the specific kinds of homework to

be assigned depending on the skills to be trained. The precise content of therapy sessions will depend on the individual patient's circumstances (the Functional Analysis). Skills tasks will be assigned at each session.

1.	Introduction, Rationale & Establish Rapport	4.	Combating Neg. Thoughts and Catastrophizing
2.	Relaxation with mindfulness meditation	5.	Stress Management & Mindfulness
3.	Habit Modification	6.	Overview & Recap

Functional analysis. IATP will employ a functional analysis of patients' pain and behavior as assessed by the PiLR system during the 2-week pretreatment ES period, and updated at study weeks 2&4. A summary of the situations that each patient encounters during ES monitoring will be reconstructed from the monitoring data, along with the accompanying mood states, cognitive appraisals and coping actions taken, and delivered to the therapist (see Fig 4). The aggregation of the multiple daily recordings will allow the therapist to detect temporal pain patterns as well as patterns in stressors (e.g., pain reliably occurs in evening, or follows negative-low arousal mood). In the Fig. 4 example it is notable that pain is worse when the subject is emotionally upset, and does little to cope. Distraction is helpful, however, as is support from friends. Early intervention with this patient might emphasize increasing sense of control and seeking support.

Figure 4. Example of Functional Analysis Chart for IATP. Chart summarizes information for multiple daily recordings, highlighting when pain occurs, and antecedent thoughts, moods, and situations.

Date		Time	Pain	Situation	Mood State	Thoughts	Actions Taken	Action effect
Patient Name: Charles F. Frost				Wk #: 1		Pre-Tx <input checked="" type="checkbox"/> Follow-up <input type="checkbox"/>		
10/01	08:15	2	At work	Pos-High = 4	Confidence =5; Control=5; Catas=0	None	3	
	12:20	2	Work break	Pos-High = 4	Confidence =3; Control=3; Catas=1	None	3	
	15:42	5	@ work; argument coworker	Neg-High = 5	Confidence =2; Control=1; Catas=3	None	2	
	21:14	5	@ home	Neg-Low = 6	Confidence=0; Control=0; Catas=4	Took PM meds	5	
10/02	08:04	3	Driving to work	Neg-Low = 3	Confidence=4; Control=4; Catas=2	Distracted self	5	
	13:08	3	Lunch	Neg-Low = 2	Confidence=3; Control=3; Catas=3	Relax jaw	0	
	19:23	4	@ home alone	Neg-Low = 6	Confidence=0; Control=0; Catas=5	None	0	
	21:44	4	@ home w friends	Neg-Low = 6	Confidence=0; Control=0; Catas=5	Distracted	3	
10/03	08:59	2	Driving to work	Neg-Low = 2	Confidence=4; Control=4; Catas=1	Distracted self	4	
	11:41	2	At work	Pos-Low = 4	Confidence=5; Control=5; Catas=0	Distracted	4	
	18:56	5	Home; Argument	Neg-High = 5	Confidence=1; Control=1; Catas=4	Nothing	0	

The prediction of emotional upsets and distraction and support coping would be early targets of treatment. It is possible that the ES records will not yield a clear pattern of antecedents to pain. In that case the therapist will ask the patient about any painful episodes that do not appear in the record, even if they do not constitute part of an identifiable pattern. The patient and therapist will work from there to determine if more coherent patterns exist. The ES records will provide a starting point for individualized treatment.

Therapists. Each therapist will possess a Master's or Doctoral degree in Psychology, Social Work, Marital and Family Therapy, or a related discipline, with at least two years' experience conducting cognitive-behavioral therapy with psychiatric patients, including pain patients.

PROCEDURE

Preparation/Training Stage (Months 1-4). During the initial phase of the project, staff will be hired and trained in the specific instruments and protocol to be used in this study. The therapists will be trained in both the manual-guided Conventional CBT, and in IATP, and in the procedures used for assigning homework and keeping documentation. Therapists will be kept blind to the specific hypotheses of the study.

Recruitment and screening. Patients will be recruited both through the University dental clinics and through newspaper, radio and internet advertisements. Persons will respond to the advertisement by telephone. Those who call will be told that the purpose of the project is to test different TMD treatments. Those interested will be screened over the telephone for basic inclusion/exclusion criteria. Those who meet eligibility at this point will be scheduled within 14 days for a diagnostic evaluation (DE).

Baseline session - DE. Persons meeting initial eligibility criteria will be consented and seen for a baseline diagnostic evaluation session. At this session potential subjects will be examined by the participating oral surgeon(s) who will rule out neuropathic or odontogenic pain and will complete the DC/TMD. Following this examination prospective subjects will have a panoramic X-ray taken to rule out gross arthritic or anatomic damage to the TM joint. The other baseline measures will then be administered, impressions will be taken for an acrylic, flat-plane disoccluding splint. Subjects will be given \$40 for completion of baseline measures.

Assignment to treatment. Those who agree to participate will be randomized to either the Standard Treatment + CBT group (STD+CBT) or to the Standard + IATP (STD+IATP) using a computerized urn randomization procedure (Stout et al., 1994). The two groups will be balanced on gender, age, ethnic background, pain level recorded at baseline, and RDC axis I diagnoses. The RA will enter the data during the DE and will inform the participant of his/her treatment assignment. The first treatment appointment will be scheduled for 2 wks later.

Training in momentary assessment using the PiLR app. After randomization, subjects in both conditions will be instructed in the use of the Program in Life Research (PiLR) app on their smartphone. Participants will use their own phones (any additional charges incurred will be reimbursed). If a patient does not have a smartphone we will provide one for the data collection episodes. Participants will be trained in the ES protocol while in the office. ES will begin on the baseline day, and will continue for the next 14 days. Participants will be told that the phone should be carried with them at all times. To promote protocol compliance participants will be told that they may receive up to \$80.00 for successful self-monitoring (\$5.00 for each successful recording day, defined as at least 3 signal-contingent recordings in a day, plus a bonus of \$5 a week for each week in which all days were recorded). This incentive procedure yielded excellent protocol compliance in our earlier studies (Litt et al., 2004; 2009). All patients will be contacted by an RA associate on their first night to discuss problems and encourage adherence to the ES.

Treatment Session 1. At this first session 2 weeks after baseline all participants will have their splints delivered and fitted by the dental assistant or oral surgeon. All participants will receive advice regarding use of the splint, advice on soft diet, and delivery of a 2-week supply of NSAIDs with written instructions. The therapist will then converse with STD+CBT patients about family and social activities until the session is over (after 45 minutes). Therapists seeing the STD+IATP patients will begin at this time with the introduction to the IATP Treatment. This first treatment session, including delivery of the splint will take about 1 hour 45 minutes for all patients.

Treatment Sessions 2 - 6. During these weekly visits subjects in the STD+IATP group will receive cognitive-behavioral treatment sessions, each about one hour in length, and directed by the prepared ES functional analysis chart (see e.g., Fig 4). STD+CBT subjects will be seen by the therapist for a brief check on progress, med adherence and splint use, plus general conversation. At sessions 2 & 4 patients will be asked to resume ES data collection via PiLR app for 7 days. At session 4 subjects in both conditions will be instructed to start to taper the use of the splint. At session 6 subjects in both groups will be asked to consider discontinuing use of the splint altogether, and asked to complete the outcome measures.

Posttreatment Data Collection. Our follow-up practices are aimed at retaining at least 80% of patients at 12mo (see Form E for **Recruitment and Retention** plans). At the 6 wks point (or after 6 sessions have been completed) patients in both groups will be asked to complete follow-versions of the dependent measures. At this point, subjects will once again be asked to participate in ES via PiLR for 7 days to determine if situation-specific coping has changed in treatment. \$25 will be offered for Post-Tx data collection + \$40 for ES for 1 wk.

Three-month Follow-up. The first follow-up data collection will take place at 3 months (post baseline). During this period all subjects will be asked to complete follow-versions of the dependent measures. In addition, subjects will once again be asked to participate in ES via PiLR app for 7 days, to determine if situation-specific changes in coping that might have occurred immediately after treatment are still in effect. \$25 will be offered for 3 Mo data collection; \$40 for Experience Sampling for 1 Week.

Later Follow-up Sessions. Follow-up data collections will take place at 6, 9 & 12mo post baseline. During these periods subjects will be asked to complete the dependent measures. A repeat ES period will also schedule for 7 days in Month 12. \$25 will be offered for 9 & 12 Mo data collection; \$40 for ES for 1 Week at 12 Mo.

Monitoring Treatment Integrity and Fidelity, and Patient Adherence to Treatment

Each session of each treatment will be guided by a Therapist Checklist to ensure that therapists address the appropriate content for that session, thus assuring fidelity to treatment. Recordings of sessions will be monitored by the therapy supervisor to assure that therapists do not stray from the treatment protocol. For all treatments, patient adherence will be measured via written records of assignments completed. Therapists will record tasks assigned and skills used each week on a skills checklist (Skills/Coping Actions Monitoring Sheet),

whether or not those skills were taught in treatment. ES response rates and tasks completed for each patient will be monitored via the PiLR system by the RAs X3 weekly. RAs will compare records with patients' assigned skills checklist (their weekly homework worked out with the therapist) to score patient adherence (Tasks completed divided by the total number of tasks assigned).

Design and Clinical Considerations

- **Therapists.** We had considered using different therapists for different treatments. However, the strong therapist effects seen in some of our earlier studies led us to use the same therapists for all conditions so as not to confound our treatment effects. This has proven to be a good strategy for us.
- **Etiologies.** Both arthralgia and myalgia patients will be included. Though the pain etiologies may be different, the pain and limits caused by these etiologies are similar and can be treated similarly.
- **Gaps in Experience Sampling.** We considered maintaining the ES throughout the treatment period with no gaps. However, the burden on patients was considered too great.
- **Clinical Applicability.** As of now, the IATP treatment is labor intensive. We are using this project to test the concept of tailored treatment for chronic pain, and to explore treatment mechanisms. If successful, clinical adaptation with adaptive, advanced mobile technology will be pursued.
- **Using Smartphone App to Deliver Treatment.** Apps are currently in development that can provide treatment suggestions in real time. This may be the next step (see above). However, such an approach would not be comparable to current usual treatment, and would not provide a good test of the hypotheses.

Data Analysis (Additional detail is provided in Form E Human Subjects).

The analyses that follow are predicated on the expectation that conventional CBT is not as efficient or effective a means of training coping skills as IATP would be. Thus IATP should perform better in the following.

- 1A, B. It is hypothesized that the STD+ IATP condition will result in significantly greater increases in reported use of coping skills on momentary basis from pre- to posttreatment relative to STD+CBT. For each person, situational recordings of coping behavior will be analyzed using multilevel modeling (Bryk & Raudenbush, 1992), which is robust against missing data. For each analysis the momentary coping score will be the repeated dependent variable, and will be analyzed as a function of time of day (coded as 1 – 4), day of the period, follow-up period (pre v. posttreatment), treatment condition (STD+CBT v. STD+IATP), and the interaction of period X condition. Significant Tx X Period effects will support the hypotheses. Pain episodes will also be compared to non-pain episodes. In particular we expect that the IATP condition will yield greater incidents of using more adaptive coping strategies, and less catastrophizing, than the CBT condition.
2. It is hypothesized that patients exposed to IATP will have better outcomes than will patients exposed to a more conventional CBT program that is not so closely individualized. Treatment effects will be analyzed using repeated measures random effects regression models. Primary Outcomes will be composite Pain Intensity Score, CES-D score, and Activity Interference Score at each follow-up point. Each analysis will take the form of a 2 group X 5 follow-up time point analysis with baseline levels of the dependent variable used as the covariate. Results will be analyzed for effects attributable to group (STD+CBT v. STD+IATP), time, and group by time. Specific contrasts will be analyzed to specify at which time point groups differ on the dependent measures. A serial gatekeeping approach (Westfall & Krishen, 2001) will be used to correct for multiple endpoints as per Turk, et al., (2008).
3. Changes in coping, catastrophization, and moods will be attributable to treatment differences, and these changes will mediate (or partially mediate) treatment effects. Multilevel mediation analyses will be used to evaluate the extent to which changes in pain, coping, and other momentary variables are (1) attributable to treatment (A path), and (2) account for treatment effects when momentary variables and Treatment effects are all in the same model (B path). A cross-products procedure with bootstrapping of standard errors as described by MacKinnon et al. (2007) and Hayes (2013) will be used to determine true mediation.
4. Additional between-subject analyses. Analyses of a more exploratory nature will also be conducted on between-subjects variables. These analyses will include the effect of dispositional moderators such as somatization, catastrophization, and neuroticism. Moderating effects will be tested by examining the interactions of these baseline measures (e.g., somatization) and Treatment on ES process measures (in this example, it may be that, by increasing attention to pain episodes, IATP may yield more somatizing responses on ES records in high somatizers than STD, and thereby have poorer outcomes for those patients). Although only 15-20% of the sample is expected to be male, moderation analyses will also include gender as a factor. We do not, however, expect differences in outcomes by gender. Measures of coping self-efficacy, and adherence to treatment will also be correlated with posttreatment outcomes to determine if these variables are

a function of specific treatment practices. Another analysis will separate those whose pain is extremely variable from those whose pain is stable at pretreatment to determine if these represent different types of patients.

5-year Study Timeline (A detailed timeline appears in From E, Section 2.7)				
Year 1	Year 2	Year 3	Year 4	Year 5
Start up, Training of therapists, Treatment of Pilot Subjects (months 1 – 4)				
Recruitment and Treatment (months 4 - 40)				
Follow-ups (months 6 – 52 including tracking late follow-ups)				
Data Analysis, Manuscript Preparation				

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