Chronic pain and cigarette smoking: The elucidation of a synergistic relationship

by

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Abstract

Chronic pain and smoking commonly co-occur, and their combination appears to have synergetic degenerative effects. While the literature investigating the association between chronic pain and smoking is relatively modest, the existent research reveals some important findings. Specifically, smoking is likely reinforced among individuals with chronic pain via the analgesic properties of nicotine, and that this effect is moderated by gender and cigarette consumption. However, little is known regarding the effects of chronic pain on factors believed to influence smoking relapse. The purpose of this study was to investigate the affect of chronic pain on nicotine withdrawal (NW) and readiness to quit (RTQ) smoking among two groups of regular smokers: those with and without chronic pain. Participants attended a baseline session (nicotine satiated) and a 24-hour nicotine deprivation session. It was hypothesized that: 1) nicotine deprivation would exacerbate pain severity, 2) NW severity would be more pronounced in the pain group, and moderated by gender, and 3) there would be a negative relationship between RTQ and the experience of chronic pain. Time invariant variables (i.e. demographics, RTQ) were collected at the baseline session, and time variant variables (i.e. NW severity, pain severity) were collected at both sessions. Data were analyzed via chi-square, ANOVA, and linear regression analyses where appropriate. Analyses revealed that, contrary to prediction, nicotine deprivation decreased pain experience in women, but did not affect pain in men. Further, no relationship was found between chronic pain, NW severity, or RTQ. The clinical and theoretical implications of these results are discussed.

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Chapter I

Introduction

Chronic pain and cigarette smoking: The elucidation of a synergistic relationship

Smoking and chronic pain constitute serious public health concerns. For example, smoking is the leading preventable cause of death in the U.S., responsible for over 400,000 premature deaths annually (National Institute on Drug Abuse [NIDA], 2009). Additionally, pain is a relatively common problem, and is associated with significant economic and healthcare costs (Pfingsten & Hidebrandt, 2004: as cited by Schneider, Schiltenwolf, Zoller, & Schmitt, 2005; Skovron, 1992). Unfortunately, these problems often co-occur. In a recent article, Borrelli (2010) defined "underserved smokers" as populations which, a) have a smoking prevalence that is 10% or greater than that of the general population, b) are at high risk for tobacco-related health problems, c) have limited access to effective treatments or have other barriers to treatment, and d) have few population-focused prospective and longitudinal treatment trials which appear in the literature. Smokers with chronic pain appear to meet these criteria. Specifically, one study estimated that 54% of individuals referred to a chronic pain clinic also smoked cigarettes (Jamison, Stetson, & Parris, 1991), which is higher than the estimated 24.2% smoking prevalence observed in the U.S. general population (NIDA, 2009). Additionally, those who suffer from chronic pain and smoke are more likely to have complications and inadequate surgical treatment outcomes compared to those who do not smoke (e.g. Vogt et al., 2002). Finally, there does not appear to be any prospective and longitudinal studies focused on the development of smoking cessation treatments for those with chronic pain in the scientific literature. Therefore, given that smokers with chronic pain represent an

important underserved population, there is a need for research that elucidates the relationship between smoking and chronic pain that can ultimately inform smoking cessation treatments. The current study examined the links between chronic pain and several factors that affect successful smoking cessation outcomes, including nicotine withdrawal and readiness to quit smoking.

Smoking and Chronic Pain

The literature investigating the relationship between chronic pain and smoking is relatively modest. However, the available literature highlights several disconcerting findings and suggests that smoking and chronic pain have a negative synergistic relationship (Andersson, Ejlertsson, & Leden, 1998; Goldberg, Scott, & Mayo, 2000; Zvolensky, McMillan, Gonzalez, & Asmundson, 2009, 2010). Highlighting this finding, a recent cross-sectional study investigated the relationship between smoking and chronic pain among a sample of German adults recruited from the general population (John et al., 2006). Smoking status, as well as pain locations (e.g. arm, head, back) and severity (1 to 9) were assessed using self-report surveys. Results indicated that current and former smokers reported more pain locations and greater pain severity compared to never-smokers. These findings are consistent with other studies using similar methodologies (Goldberg et al., 2000; John et al., 2009; Kamaleri, Natvig, Ihlebaek, Benth, & Bruusgaard, 2008). Further, research investigating the inverse of the smoking-pain relationship has found similar results. Specifically, it has been observed that individuals who report suffering from chronic pain are also at a higher risk for smoking cigarettes compared to their peers who do not suffer from chronic pain (Jamison et al., 1991; Zvolensky et al., 2009, 2010).

The synergistic relationship between smoking and chronic pain is particularly troublesome given that smoking behavior, in addition to other well documented health consequences, may lead to accelerated bone loss, spinal disk degeneration, and restricted blood flow to discs and other vertebral tissues which can exacerbate the experience of pain (Vogt et al., 2002). Additionally, smoking and chronic pain are related to a number of negative health indicators. Specifically, smokers with chronic pain are more likely to use pain medications compared to their non-smoking peers (Barton, Kofoed, & Doleys, 1989; Jamison et al., 1991), and are less likely to experience pain improvement following spinal surgery (Vogt et al., 2002). Furthermore, smoking and chronic pain are both associated with psychological dysfunction (e.g. depression, anxiety: Fishbain et al., 2007; Kamaleri et al., 2008; Morrell & Cohen, 2006).

Smoking and Analgesia

Given the serious health consequences of smoking, which are compounded among those who experience chronic pain, it is critical to gain a better understanding of the factors that reinforce smoking behavior in this population. Recent evidence suggests that the experience of pain increases craving to smoke and reduces latency to smoke following painful cold pressor procedures when compared to non-painful cold pressor procedures (Ditre & Brandon, 2008). This finding suggests that smoking may affect the experience of pain or provide a means of coping. The notion that nicotine affects the experience of pain has been generally supported in the literature, with findings from studies using various indicators of pain suggesting that nicotine moderates the pain experience.

The existing literature on the moderating affects of nicotine on pain suggests a number of important findings. First, nicotine administration generally decreases the experience of pain. This finding has been observed in laboratory (e.g. Girdler et al., 2005) and community-based research (e.g. John et al., 2009). Specifically, laboratory studies have found that nicotine administration (via smoking, snuff, or nicotine nasal spray) increases pain threshold (i.e., the point at which pain is first detectable) and pain tolerance (i.e., the maximum level of pain one can willingly withstand) (Girdler et al., 2005; Jamner et al., 1998; Lane et al., 1995). These findings are consistent for a variety of pain induction techniques including thermal pain (heat), cold pressor (submersion of arm in to ice water), and tourniquet ischemia (halting limb blood circulation using a blood pressure cuff). However, research eliciting pain from electric shock has demonstrated mixed findings (Jamner et al., 1998; Knott, 1990; Sult & Moss, 1986), suggesting that nicotine may not moderate the experience of all types of pain. Community based studies have also supported the link between pain and nicotine. Specifically, it has been demonstrated that heavy smokers report less severe pain than lighter smokers (John et al., 2009), suggesting an analgesic effect at greater levels of nicotine consumption.

A second important finding is that the analgesic effects of nicotine administration appear to be independent of withdrawal reduction (Fertig, Pomerleau, & Sanders, 1986). Specifically, Fertig and colleagues (1986) noted that nicotine administration increased pain tolerance and the latency of pain detection. It was also observed that overall pain severity decreased when nicotine was administered; however, it did not appear to affect withdrawal severity in minimally deprived smokers. This, and other studies (e.g.,

Pomerleau, Turk, & Fertig, 1984), suggest that nicotine's analgesic effect is not a function of withdrawal symptom reduction. This is an important finding as it suggests that pain and nicotine withdrawal are distinct constructs, and can be measured and manipulated independently.

A third finding suggests that nicotine's analgesic effects are not constant across all types of pain. Specifically, while nicotine moderates muscular skeletal pain (i.e. structural damage), it does not appear to moderate neuropathic pain (i.e. pain caused by damaged or dying nerves). Specifically, Bendow, Williams, and MacFarlane (1997) found no evidence for an analgesic effect of nicotine among individuals who suffered from pain resulting from diabetic neuropathy. This finding suggests that individuals with neuropathic pain may smoke for reasons other than pain management.

Finally, there appears to be a complex dose/response relationship between nicotine consumption and analgesia (Jamner et al., 1998). Specifically, Knott (1990) found a negative correlation between nicotine consumption (measured via expired CO) and subjective markers of pain in female smokers. On the other hand, several other researchers have found positive relationships between smoking consumption (measured via number of pack years and years smoking), level of nicotine dependence, and pain severity (Goldberg et al., 2000; John et al., 2009; Scott, Goldberg, Mayo, Stock, & Poîtras, 1999; Weingarten et al., 2008; Zimmermann-Stenzel, Mannuay, Schneider, & Schiltenwolf, 2008). While these results may appear contradictory, one interpretation is that as pain severity increases, use of nicotine for analgesic purposes must also escalate to compensate.

Gender and Nicotine Analgesia

While the majority of early studies demonstrated that nicotine attenuates the experience of pain, several studies that followed have either failed to find this effect or found only modest relationships (Perkins et al., 1994; Sult & Moss, 1986). One factor which may help to explain these mixed findings is gender. Specifically, it has been suggested that the analgesic effects of nicotine differentially affect men and women. In a well-cited study, Jamner and colleagues (1998) investigated the relationships among pain perception, nicotine administration, and gender. Using electrical stimulation to induce pain among a large sample of male and female smokers and non-smokers, they found that nicotine (administered via nicotine patch) increased pain threshold in men but not in women (Jamner et al., 1998). These findings were later replicated and expanded by Girdler and colleagues (2005) who also investigated the relationships between pain (induced via thermal, cold pressor, and tourniquet ischemia), gender, and nicotine (administered via paced smoking). However, in this study, it was observed that gender differences were dependent on the type induction technique, with women demonstrating a nicotine analgesic effect with ischemic pain, and men demonstrating this effect with cold pressor pain (no gender differences were found for thermal pain). Consequently, the authors suggested that these findings were likely the result of differential neuroendocrine mechanisms (e.g. decreased estrogen concentrations in female smokers and increased plasma norepinephrine in male smokers). The authors concluded that the mixed findings regarding nicotine analgesia, pain, and gender in the literature are likely the result of varied study methodologies (including pain induction) and a failure to include a sufficient number of women for gender analysis. However, this conclusion should be noted with

caution as Gridler and colleagues (2005) did not include pain from electrical stimulation in their study. Further, the finding with regard to thermal pain induction was inconsistent with previous findings (Lane et al., 1995). Therefore, while much of the available literature supports the notion that the analgesic effects of nicotine are more pronounced in men than women (Jamner et al., 1998), and that the analgesic process of nicotine affects a broader range of pain in men (i.e. cold pressor, electrical stimulation, thermal pain) compared to women (ischemic pain; Jamner et al., 1998; Perkins et al., 1994), further research is clearly needed to elucidate the implications of gender on nicotine use and the experience of pain.

Readiness to Change and Nicotine Analgesia

As highlighted above, smoking is likely reinforced among individuals who suffer from chronic pain given nicotine's analgesic effects (Girdler et al., 2005; Jamner et al., 1998; Lane et al., 1995). As a result, analgesia from nicotine likely makes smoking cessation treatment problematic among this population, especially if chronic pain treatments do not provide adequate relief. Therefore, it seems logical to assume that the experience of chronic pain affects smokers' readiness to change their smoking behavior. Prochaska, DiClemente, and Norcross (1992) defined 5 stages that outline the process of behavior change. These stages include the pre-contemplation, contemplation, preparation, action, and maintenance stages. These stages of change are important as they have been shown to have direct treatment implications for smoking cessation in the general population (Spencer, Pagell, Hallion, & Adams, 2002). However, the usefulness of this model for those with chronic pain is unknown, as the previous literature investigating the

relationship between readiness to change and chronic pain contains significant methodological flaws.

In a cross-sectional survey study, Hahn, Rayes, Kirsh, and Passik (2006) investigated the relationship between markers of pain severity and stage of change among 307 adults who reported using tobacco products (i.e., cigarettes, pipes, cigars) within the past 30 days. Using a subsample that reported significant pain (i.e., pain more severe than typical headaches and toothaches) during the past week, experience of pain was compared to stage of change. Results revealed no relationship between experience of pain and stage of change. However, numerous methodological flaws were present in this study. First, the sample included a large proportion of light smokers who likely did not meet criteria for nicotine dependence. Specifically, only 30% of the sample reported smoking more than one pack per day and 13% reported smoking zero cigarettes/day. Additionally, the research group defined pain experience as any pain "beyond the usual minor headaches, sprains, or toothaches" (p. 476) during the past week. This definition of pain allows for the inclusion of individuals who experience both acute and chronic pain. This is problematic, as the negative reinforcing analgesic effects of nicotine likely take time to learn, and may not be seen in individuals experiencing acute pain.

Burkhalter, Springer, Chhabra, Ostroff, and Rapkin (2005) also investigated the relationship between readiness to change and pain. Their study included a sample of HIV-infected individuals, and found that the experience of pain was unrelated to readiness to quit smoking. However, similar to Hahn and colleagues (2006), they failed to consider the possible relationship between the chronic nature of pain and readiness to change. Additionally, as noted in their introduction, individuals with HIV disease

typically have a “high prevalence of smoking” and a “low readiness to quit” (p. 512) likely limiting sample variability, and thus the ability to find a relationship between readiness to quit and other variables. In sum, the relationship between chronic pain and readiness to quit smoking remains largely unresolved and further research is needed.

Chronic Pain and Nicotine Withdrawal

Nicotine withdrawal is an important barrier to successful smoking cessation, as avoidance of withdrawal symptoms have been shown to motivate nicotine use and relapse (Allen, Bade, Hatsukami, & Center, 2008). Further, withdrawal severity has been associated with latency to relapse and cessation success (Madden et al., 1997; Xian et al., 2003). Unfortunately, little is known regarding the relationship between chronic pain and the experience of nicotine withdrawal. Results from two studies, however, suggest that these processes may be related. Andersson, Ejlertsson and Leden (1998) investigated the link between musculoskeletal pain and smoking. In a cross-sectional study, the authors observed that widespread pain was associated with increased depression, difficulty relaxing, sleep disturbance, and fatigue. Interestingly, these symptoms overlap with the symptoms listed for Nicotine Withdrawal in the DSM-IV-TR (American Psychiatric Association [APA], 2000). It is possible therefore, that individuals experiencing chronic pain will have an increased sensitivity to these symptoms during periods of nicotine abstinence. In a more recent study, John, Meyer, Rumpf, and Hapke (2009) investigated the associations amongst the experience of pain, criteria for Nicotine Dependence, and nicotine withdrawal symptoms. This cross-sectional survey study included adults from northern Germany, and used the DSM-IV-TR criteria to assess nicotine dependence and nicotine withdrawal (which is part of the dependence criteria). Pain was operationalized

using ordinal pain categories that combined pain severity (# of pain sites) and chronicity. Results revealed positive relationships between pain severity and number of endorsed DSM-IV-TR nicotine dependence criteria, and between pain severity and number of endorsed DSM-IV-TR nicotine withdrawal symptoms. As a result, the authors concluded that nicotine dependence predicts increased pain. While the findings from these studies suggest a relationship between nicotine withdrawal severity and the experience of pain, neither provides a direct comparison between these two constructs. Specifically, Andersson and colleagues (1998) did not assess nicotine withdrawal as they were investigating the effects of smoking on chronic pain. Additionally, John and colleagues (2009) did not make a direct comparison between pain and withdrawal severity as they compared pain experience to nicotine dependence criteria and nicotine withdrawal symptom breadth (not severity). Therefore, while there is some indirect evidence to suggest that a link exists between the experience of pain and nicotine withdrawal, the relationship between these two constructs remains untested.

Current Study

Given that many chronic pain suffers who smoke are interested in quitting smoking (Hooten et al., 2009), the primary goal of this study is to examine several possible mechanisms of smoking relapse among individuals who suffer from chronic pain. Specifically, the proposed study examined the affects of chronic pain on the experience of nicotine withdrawal and readiness to quit smoking among two community samples of nicotine dependent smokers: those who currently suffer from chronic muscular-skeletal pain and those who are pain free. This study also investigated the roles of two possible moderators of the relationship between muscular-skeletal pain and

smoking, including gender and smoking consumption. The proposed study was designed to assess these processes during a period of smoking satiation and following a 24-hour nicotine deprivation period.

Hypothesis

1) Participants from the chronic pain sample will experience a significant increase in muscular-skeletal pain severity following the smoking deprivation period compared to the satiation period. This finding will be moderated by gender, with men showing greater increases in pain compared to women. This finding would suggest that nicotine acts as an analgesic, which is consistent with previous laboratory findings. Further, this finding would extend the literature by providing an ecologically valid assessment of the effects of nicotine deprivation on the experience of chronic pain. Pain severity will be measured via the continuous pain scale from the McGill Pain Questionnaire, and smoking abstinence will be confirmed via respiratory CO.
2) Smokers who experience chronic muscular-skeletal pain will report more severe nicotine withdrawal and nicotine craving during abstinence compared to the control group. This finding would be consistent with the previous cross-sectional finding that the experience of pain is related to the breadth of self-reported nicotine withdrawal symptoms (John et al., 2009). However, this finding would extend the literature by allowing for causal inferences to be drawn, and for the assessment of withdrawal symptom severity as well as breadth.
3) Male smokers with chronic muscular-skeletal pain will report greater withdrawal severity and nicotine craving compared to female smokers with chronic muscular-

skeletal pain during the abstinence period. These findings will be moderated by smoking level, with individuals reporting higher pack years demonstrating more severe nicotine withdrawal and nicotine craving. This finding would strengthen the assertion that the analgesic effects of nicotine are more consistent in men than women, while also providing an ecological assessment of these constructs.

4) Among those participants with chronic pain, the experience of nicotine withdrawal will be positively related to the experience of muscular-skeletal pain, but unrelated to neuropathic pain experience. This finding would be consistent with the results of Bendow and colleagues (1997), who found that smoking was unrelated to the experience of diabetic neuropathic pain. This finding would also extend the literature as it will allow for a direct ecological comparison of the experience of muscular-skeletal and neuropathic pain following nicotine withdrawal.
5) Given that smoking produces an analgesic effect, there will be an inverse relationship between pain severity and readiness to quit smoking as measured by the stages of change (Prochaska et al., 1992). This effect will be moderated by gender (i.e., men demonstrating a stronger relationship compared to women) and smoking quantity (i.e., high pack years relating to a stronger relationship compared to low pack years). Readiness to quit smoking will be measured via the Contemplation Ladder (Biener & Abrams, 1991), which provides an assessment consistent with the stages of change model. The current study will provide a better test of this relationship than what has been previously reported in the literature

(i.e. Burkhalter et al., 2005; Hahn et al., 2006), as it will include a sample of participants who experience chronic pain and who are also nicotine dependent.

Chapter 2

Methods

Participants

A pre-study power analysis was conducted using G*Power (v. 3.0.10). This analysis recommended a sample size of 24 participants per group (48 total participants), given a moderate effect size to reach a statistical power of .80 at the p=.05 level. The final sample consisted of 21 smokers, including 14 in the chronic pain group and 7 in the non-pain group. The final sample was smaller than that recommended by the power analysis given recruitment difficulties[1] (see Appendix B which outlines study recruitment difficulties). The final sample was 66.7% male, 76.2% Caucasian, 9.5% Hispanic, 4.8% African American, 4.8% Native American, and 4.8% other. At intake, participants were screened for general inclusion criteria which included an age of 18 years or older (*M* = 46.8 years, *SD* = 11.7 years), average consumption of 16 or more cigarettes a day over the past 6 months (*M* = 23.1 cigarettes/day, *SD* = 8.9), a Fagerström Test for Nicotine Dependence [FTND] score of 5 or greater denoting at least moderate dependence (*M* = 7.1, *SD*= 1.4), and a respiratory CO level of 10 parts per million [ppm] or greater at intake (*M* = 23.19, *SD* = 7.96). Additionally, participants must have met the specific inclusion recruitments for either the pain or non-pain group. Participants qualified for the chronic pain group if they reported significant continuous pain over the past 3 months, and scored in the "average" to "above average" ranges (i.e., score of 22 or greater) for continuous pain on the Short Form McGill Pain Questionnaire, average version (SF-

[1] Data collection for the purpose of this dissertation concluded on May 1st, 2011. This end date was approved by the dissertation committee on February 19th, 2011. However, data collection continues for this study, and the data will be reanalyzed once the target sample size is reached.

MPQ-2, average). Participants qualified for the control group if they had not experienced continuous pain over the past 3 months, and scored in the "below average" range (i.e., score of 21 or less) for continuous pain on the SF-MPQ-2 (average version). Study exclusion criteria included evidence of current or past diagnosis of a psychotic disorder, mania or hypomania, mental retardation, dementia, multiple sclerosis, or Parkinson's disease.

Procedure

Participant recruitment and screening.

Participants were identified via two methods. First, participants were identified and recruited though the various Family Medicine clinics at the Texas Tech University Health Sciences Center (TTUHSC). Specifically, clinic personnel reviewed patient charts to identify participants who likely met study inclusion criteria (e.g. current smokers). Clinic personnel reviewed the following sections of patients' medical records to assess smoking and pain status: current diagnosis, past diagnosis, problem list, and notes. Patients whose medical records indicated that they were a current smoker were approached and screened by study personnel before, during, or following (prior to leaving the clinic) their medical appointment. Qualifying participants were then consented and scheduled for study participation. Second, study recruitment flyers were posted at the TTUHSC and ads were run in a local newspaper. Potential participants were asked to call study personnel for screening if they were interested in participating. Qualifying participants were subsequently scheduled for a face-to-face meeting during which time they were consented. This second recruitment method was initiated approximately 10

months into data collection due to slow study recruitment and high attrition rates (see Appendix B for a description of study recruitment challenges).

The study screening procedure consisted of 3 self-report surveys (administered either over the phone or in-person depending on recruitment method) including the FTND, the SF-MPQ-2 (Note: some participants completed the SF-MPQ-2 measure as part of their standard medical care and were not be asked to repeat this measure), and a brief questionnaire including smoking and pain history questions. Additionally, participants were asked to exhale into a monitor designed to measure their CO level. Informed consent was obtained during face-to-face meetings. Participants were given the informed consent document and provided the opportunity to ask questions. Comprehension of the document was assessed by having participants describe the study in their own words. Following completion of the consent and screening process, participants who qualified were scheduled for two experimental sessions, including a smoking satiation (study session #1) and 24-hour deprivation session (study session #2).

Experimental study sessions.

Study session #1: nicotine satiation condition.

Upon arrival to the clinic, participant's CO levels were measured. Participants were then escorted to an approved smoking location and asked to smoke one of their preferred cigarettes. If participants did not have cigarettes available, a cigarette was provided by study personnel. This procedure standardized the time of last cigarette smoked and minimized any affects of nicotine withdrawal. Once participants completed smoking their cigarette, they were escorted back to the Family Medicine Clinic where they were seated in a private room and the following counterbalanced

measures/interviews were administered: substance use disorders modules from the Mini International Neuropsychiatric Interview (M.I.N.I.), a self-report assessment packet which included a background questionnaire created for the propose of this study, the Contemplation Ladder (CL), the Personality Assessment Inventory (PAI), the Center for Epidemiologic Studies-Depression Scale (CES-D Scale), the Nicotine Withdrawal Symptoms Checklist (NWSC), the SF-MPQ-2 (current), and the Quality of Life Inventory (QoLI). As this assessment is was lengthy, participants were provided multiple opportunities to take short breaks. Additionally, participants were permitted to smoke another cigarette if they expressed the need to do so. Following competition of the self-report assessment participants were asked to provide a urine sample to assess current drug use (i.e. marijuana, cocaine, amphetamines, opiates, and benzodiazepines). Following the collection of the urine sample, participants were instructed to abstain from smoking until their next visit, which was scheduled for 24 hours following their last cigarette. Participants were reminded that abstinence would be verified via respiratory CO levels. Finally, participants were provided with a handout that offered coping strategies designed to help them successfully abstain from smoking. All participants were compensated $10 for session #1. After the participants were excused from the satiation session, medical information, including current and past diagnoses and medications, were collected from each of the participant's electronic medical record (medical record data collection sheet), and the urine analysis was conducted.

Session #2: nicotine deprivation condition.

Upon arrival to the deprivation session, CO levels were assessed to confirm smoking abstinence. Participants returning a CO level of less than 10 ppm, or a CO level

that had decreased 50% from baseline (for those who returned baseline CO levels greater than 20 ppm only) were considered abstinent. Participants who did not meet either of these criteria were invited to restart their deprivation period a week later (see abstinence reattempt session below). Following the CO assessment, abstinent smokers were administered the following counterbalanced measures: the NWSC, the SF-MPQ-2 (current), and a current medication use survey.

Participants were compensated for the deprivation session (session #2) based on their effort, and received up to $40 total. Specifically, participants were compensated $10 each time they attempted the deprivation period and attended the scheduled appointment (a maximum of 3 failed attempts were allowed). Once a participant achieved successful smoking abstinence (as defined by the CO criteria above), they received a bonus which made their total deprivation session compensation worth $40. For example, a participant who was successfully abstinent on their first attempt received $10 for attending the session, and a $30 bonus. A participant who was successfully abstinent after 2 attempts received $10 for attending each of their 2 deprivation sessions ($20), and a $20 bonus. Finally, a participant who was successful in achieving smoking abstinence after 3 attempts received $10 for attending each of their 3 deprivation sessions ($30), and a $10 bonus. Participants who were not able to remain abstinent for the 24-hour period were compensated a total of $30 for attending their deprivation sessions.

Following the completion of both experimental sessions, participants were debriefed as to the study aims and were provided with smoking cessation resources including informational brochures and a smoking cessation hotline number.

Abstinence re-attempt.

Participants who were unable to abstain from smoking during the deprivation period, or who failed meet the deprivation CO requirements, were invited to try again one week following their failed abstinence attempt. In such cases, participants were required to present for two consecutive days. On the first day, participants' CO levels were reassessed. Participants were then escorted to an approved smoking location and asked to smoke one of their preferred cigarettes. If participants did not have cigarettes available, a standard cigarette was provided by study personnel. Again, this procedure standardized the time of the last cigarette smoked, and minimized any effects of nicotine withdrawal. Upon completion of the cigarette smoking procedure, participants were escorted back to the Family Medicine Clinic where they completed the NWSC and the SF-MPQ-2 (current). This reassessment allowed for a standardized measurement of participant's baseline levels. Participants were then asked to abstain from smoking cigarettes for 24 hours and another deprivation session was scheduled for 24-hours later. Participants were allowed to attempt the smoking deprivation condition three times. Following a failed third deprivation attempt participants were excused from the study.

Assessments.

Demographic information.

Demographic and background information was collected via a survey designed for the purpose of this study (see Appendix C). This information was administered to allow for a thorough description of the sample, as well as to control for possible differences between the chronic pain and control groups.

Smoking history and nicotine dependence.

Information regarding smoking history was collected via a survey designed for the purpose of this study (see Appendix C). This survey inquired about past smoking behavior including duration of smoking, smoking quantity, and past quit attempts.

Fagerström Test for Nicotine Dependence (FTND; Heatherton, Kozlowski, & Frecker, 1991). Nicotine dependence was assessed via the FTND (see Appendix D). The FTND is a 6-item self-report measure of behaviors typically associated with nicotine dependence (e.g. "How soon after you wake up do you smoke your first cigarette?", "Do you find it difficult to refrain from smoking in places where it is forbidden?"). Each item is rated on a 0 to 1 or 0 to 3 point scale (depending on the question), with higher scores indicative of higher levels of nicotine dependence. The measure yields a maximum possible score of 10, with a score of 5 indicating moderate dependence (Fagerstrom, Heatherton, & Kozlowski, 1990). The FTND is a commonly used measure of nicotine dependence, and has been shown to have adequate test-retest reliability and internal consistency (C. Pomerleau, Carton, Lutzke, Flessland, & Pomerleau, 1994).

Nicotine withdrawal and craving.

Nicotine Withdrawal Symptoms Checklist (NWSC; Hughes, Hatsukami, Mitchell, & Dahlgren, 1986). Nicotine withdrawal was assessed using the NWSC (see Appendix E). The NWSC is a 12-item self-report measure of nicotine withdrawal severity which includes commonly measured nicotine withdrawal symptoms (11 items) and craving (1 item). Each item is rated on a 4-point Likert scale of symptom severity ranging from 0 to 3 (not present to severe). A withdrawal symptom total severity score was calculated by summing items 2 through 12, yielding a severity score ranging from 0 to 33.

Pain history and severity.

Pain history was assessed via questions included on the demographic survey (see Appendix C). This survey included questions regarding past experience(s) of pain, including cause of pain, previous treatments (including medications), duration, and severity.

Short Form McGill Pain Questionnaire (SF-MPQ-2; Dworkin et al., 2009). Pain severity was measured using the SF-MPQ-2 (see Appendix L). The SF-MPQ-2 is a 22-item self-report assessment tool designed to provide a comprehensive measurement and characterization of the experience of neuropathic and non-neuropathic pain (Dworkin et al., 2009). SF-MPQ-2 items are rated on an 11-point Likert scale ranging from 0 to 10 (none to worst possible). The SF-MPQ-2 contains 5 subscales, including the continuous (sum of 6 items, score range 0 to 60), intermittent (sum of 6 items, score range from 0 to 60), neuropathic (sum of 6 items, score range from 0 to 60), affective descriptors (sum of 4 items, score range from 0 to 40), and total pain scales (sum of 22 items, score range from 0 to 220). Higher subscale and total scores are indicative of greater pain severity. For the purpose of this study, the continuous pain subscale was used as a marker of non-neuropathic, musculoskeletal pain severity, as this scale has been shown to be less sensitive to the experience of neuropathic pain (Dworkin et al., 2009). This survey has adequate internal consistency, with average subscale Cronbach's alphas ranging between 0.73 and 0.95 (Dworkin et al., 2009). This measure was normed using a sample of chronic pain patients, therefore, t-scores are interpreted in the context of other chronic pain patients. Two versions of this measure were administered during this study, including the standard version which assesses average levels of pain (see Appendix F),

and a modified version which will assess participants' current experience of pain (see Appendix G).

***Readiness to change*.**

Contemplation Ladder (CL; Biener & Abrams, 1991). Motivation to quit smoking was assessed via the CL (see Appendix H). The CL is a single item self-report measure which assesses readiness to change on an 11-point vertically displayed, Likert scale ranging from 0 to 10 (No thought of quitting - Taking action to quit). The CL was designed to be complementary to the stages of change model (Prochaska & DiClemente, 1983), but quantifies readiness to change on a continuum and not as discrete stages. Consistent with this, the CL has been shown to have good convergent validity with the University of Rhode Island Change Assessment, which assesses readiness to change in terms of discrete stages (Amodei & Lamb, 2004). The CL has also demonstrated good concurrent validity, as it has been shown to distinguish between known groups, specifically between those who plan to quit in the next month and those who have no plans to quit (Amodei & Lamb, 2004; Biener & Abrams, 1991).

***Mental health and personality*.**

*Personality Assessment Inventory (*PAI; Morey, 1991). Considering that pain and smoking are related to psychological dysfunction (Fishbain et al., 2007; Kamaleri et al., 2008), the PAI was used to assess participants' general psychological functioning. This assessment allowed for an enhanced description of the sample, as well as a control for possible group differences. The PAI is an objective self-report measure designed to assess personality and psychological functioning of individuals 18-years and older. The PAI is comprised of 4 types of scales, including 4 validity scales, 11 clinical scales, 5

treatment scales, and 2 interpersonal scales. The PAI consists of 344 items rated on a 4-point Likert scale from *False* to *Very True*. This assessment tool has been validated and normed using both clinical and non-clinical (community and college) samples. Validation studies have generally found that the validity, clinical, treatment, and interpersonal scales of the PAI have adequate convergent and discriminant validity, as well as adequate internal consistency (α range .22 to .94) and test-retest reliability (r range .29 to .94) (Morey, 2007; PAI Manual).

Quality of Life Inventory (QoLI: Frisch, Cornell, Villanueva, & Retzlaff, 1992). Given that impaired quality of life is often associated with chronic pain, the QoLI was used to describe and control for possible group differences between groups. The QoLI is a 32-item self-report measure which assesses the quality of multiple life domains including health, self-esteem, goals and values, money, work, play, learning, creativity, helping, love, friends, children, relatives, home, neighborhood, and community. Each life domain is measured by multiplying an "importance" rating by a "satisfaction" rating specific to each domain. This yields life domains scores that range from -6 (very low quality) to 6 (very high quality).

Center for Epidemiologic Studies- Depression Scale (CES-D; Randloff, 1977). Given that symptoms of depression are common to both pain and nicotine withdrawal (APA, 2000; Andersson, Ejlertsson & Leden, 1998), the CES-D was administered to identify differences in baseline symptoms of depression between the pain and non-pain groups. The CES-D is a 20-item self-report measure that assesses for common symptoms of depression (e.g. low mood, sleep disturbances, appetite changes). Items are rated on a 4-point Likert scale assessing symptom frequency ("Rarely or none of the time" to "Most

or all of the time") over the previous week. The CES-D has been shown to have adequate convergent and discriminant validity, as well as internal consistency (α range .84 to .90) and test-retest reliability (r range .45 to .70) (Randloff, 1977).

Substance use, current and past.

Given the strong association among co-morbid pain, smoking, and drug use (Barton et al., 1989; Jamison et al., 1991), as well as the affects of drug use (both prescription and recreational) on the experience of pain, current and past substance use was assessed via multiple means. This assessment allowed for a complete description of the sample and to control for potential group differences. Substance use assessments are described in detail below.

Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1992). The M.I.N.I. substance use dependence modules were used to assess for current substance dependence or abuse. The M.I.N.I. is a structured clinical interview designed to increase the accuracy and efficiency of clinical assessment and diagnosis. The substance use disorders model assesses for substance abuse and dependence during the past 12 months, and is based on DSM-IV-TR criteria (APA, 2000). Substances assessed in this module include stimulants, cocaine, narcotics, hallucinogens, inhalants, marijuana, tranquilizers, and other miscellaneous substances (e.g., diet pills, steroids).

Current Medication Use Survey. The current medication use survey was created for this study, and was used to assess use of pain medication prior to the smoking deprivation period (see Appendix K). Current medication use was assessed, as pain medications may influence withdrawal and pain severity.

Urine Toxicology Screening. A 5-panel urine toxicology screen (American Screening Corporation, Shreveport, LA, USA) was used to biochemically verify drug use. Specifically, participants were asked to provide a urine sample which was analyzed for the presence of cocaine, THC, amphetamines, opiates, and benzodiazepines. The 5-panel urine toxicology screen is sensitive to cocaine at 300 ng/mL, THC at 50 ng/mL, amphetamines at 1,000 ng/mL, opiates at 2,000 ng/mL, and benzodiazepines at 300 ng/mL.

Past substance use was also assessed via questions included on the demographic questionnaire noted above (see Appendix C).

Smoking status.

Participants' smoking status, as well as abstinence from smoking, was biochemically verified through respiratory carbon-monoxide (CO) using a Vitalograph Breath CO monitor (Model 2900: Vitalograph, Lenexa, KS, USA). According to the guidelines set forth by the Society for Research on Nicotine and Tobacco's Subcommittee on Biochemical Verification (2002), the optimal CO cut-off level to distinguish regular tobacco users from non-users is between 8-10 ppm. Therefore, it was required that all qualified participants return a CO level of 10 ppm or greater to confirm their smoking status. During the deprivation condition, abstinence was verified using one of two criteria. First, any participant returning a CO level of less than 10 ppm was considered abstinent for the past 24 hours. Second, participants who returned high CO levels at baseline (above 20 ppm) were considered abstinent if they demonstrated a drop in CO level of at least 50%, even if their deprivation reading was greater than 10 ppm.

The second criterion has been used in several studies (e.g. Tidey, Higgins, Bickel, & Steingard, 1999).

Additional smoking history information was collected via questions included on the background questionnaire noted above (See Appendix C).

Current and past diagnosis and treatment information.

Current and previous diagnosis and treatment information (i.e. medications and procedures) was collected to allow for a description of the sample, as well as to control for possible groups differences. This information was collected via two methods. First, information was obtained from each participant's medical record (medical record data collection sheet). Second, as information from any participant's medical record is not likely to contain all previous diagnosis and treatments, this information was augmented by self-report. Self-report information was collected through the demographic use questionnaire described above (See Appendix C).

Data Analysis

Descriptive statistics (means, standard deviations, and frequencies) were calculated for age, education, marital status, ethnicity, substance use history, cigarette consumption, years smoked, respiratory CO level, FTND score, SF-MPQ-2 scores, and medical conditions. Descriptive statistics were also used to describe the sample in terms of psychological functioning as measured by the PAI. Additionally, a series of one-way Analysis of Variance (ANOVA) and chi-square analyses were used to test for possible group differences that could confound results.

Where appropriate, hypothesis were tested via paired samples t-tests, or analysis of variance (ANOVA) in which pre-to-post test change scores were calculated for pain

severity (SF-MPQ-2, current), nicotine withdrawal symptom severity (NWSC), and nicotine craving (QSU). Data were also analyzed via regression analyses.

Chapter III

Results

Descriptive Analyses

Study sample demographic, substance use, smoking, and pain data are presented in Tables 1 through 5. Overall, analyses of demographic data revealed that the chronic pain and non-pain samples were similar in most respects, and that the majority of observed differences (i.e. pain severity and PAI- Somatization clinical scale) were consistent with the study design. However, analyses revealed that the chronic pain and non-pain samples differed in two unanticipated ways. Specifically, the non-pain group was observed to have higher scores on both the PAI Antisocial and Alcohol clinical scales.

Analyses of Study Hypotheses

Hypothesis 1.

Hypothesis 1 predicted that the chronic pain group would show a significant increase in musculoskeletal pain severity following nicotine deprivation, and that this effect would be moderated by gender. Musculoskeletal pain was measured via the continuous pain subscale on the SF-MPQ-2 (current) and the subjective pain questionnaire. The main effect of pain was analyzed via paired samples t-test comparing pre and post deprivation pain scores. The interaction between pain and gender was analyzed via one-way ANOVAs comparing pre-to-post pain change scores by gender. Analyses revealed no main effect of pain severity pre-to-post deprivation as reported by the SF-MPQ-2 [$t(13) = 1.78$, $p = .09$] or the subjective pain questionnaire [$t(13) = 0.27$, $p = .78$]. However, there was a significant interaction observed between pre-to-post pain

experience and gender on the SF-MSQ-2 [$F(1,12) = 8.93$, $p = .011$], but not on the subjective pain questionnaire [$F(1, 12) = 0.25$, $p = .63$]. Contrary to what was expected, the significant interaction between pain severity and gender revealed that, women showed a significant decrease in pain severity as reported by the SF-MPQ-2, while men evidenced no change (see Figure 1).

Statistical assumptions for hypothesis 1 analysis were tested via reviews of appropriate graphs and statistical tests (e.g. Levene homogeneity of variance tests). The only assumption violated during these analyses was the assumption of randomization to condition (ANOVA).

Hypothesis 2.

Hypothesis 2 predicted that smokers with chronic pain would show greater increases in total withdrawal severity and nicotine craving following smoking abstinence compared to smokers without chronic pain. Total withdrawal severity and nicotine craving were assessed using the NWSC and QSU respectively. As a manipulation check, nicotine withdrawal and craving scores were analysis via paired samples t-test comparing pre and post deprivation assessments for the entire sample. Hypothesis 2 was tested via two one-way ANOVAs comparing withdrawal and craving change scores between groups. The manipulation check revealed that, as expected, NWSC [$t(20) = -4.79$, $p < .001$] and QSU [$t(20) = -4.43$, $p < .001$] scores significantly increased pre-to-post deprivation. However, no interaction between pain status (no pain versus chronic pain) and either nicotine withdrawal severity [$F(1,19) = .06$, $p = 0.80$] or nicotine craving severity [$F(1,19) = 0.58$, $p = .46$] was observed. Therefore, contrary to prediction, there

were no differential changes in nicotine withdrawal or craving severity by pain status (see Figures 2 and 3 respectively).

Statistical assumptions for the hypothesis 2 analysis were assessed via reviews of appropriate graphs and statistical tests (e.g. Levene homogeneity of variance tests). The only assumption violated during these analyses was the assumption of randomization to condition (ANOVA).

Hypothesis 3.

Hypothesis 3 predicted that male smokers with chronic pain would show a greater increase in total withdrawal severity and nicotine craving following smoking abstinence compared to their female counterparts. Additionally, this hypothesis predicted that the relationship between withdrawal/craving and gender would be moderated by pack years. Total withdrawal severity and nicotine craving were assessed with the NWSC and QSU. This hypothesis was tested via two one-way ANOVAs comparing withdrawal and craving change scores to gender and pack years (using a median split) among the chronic pain group. Analyses did not reveal significant main effects between nicotine withdrawal changes scores and either gender [$F(1,10) = 0.003$, $p = .96$] or pack years [$F(1,10) = 0.49$, $p = .49$]. Additionally, a significant interaction between gender and median split pack years was not observed [$F(1,10) = 0.003$, $p = .96$] (see Figure 4). Likewise, analyses also did not reveal significant main effects between nicotine craving change scores and either gender [$F(1,10) = 0.011$, $p = .92$] or pack years, [$F(1,10) = 1.78$, $p = .21$]. Further, a significant interaction between gender and pack years was not observed [$F(1,10) = 2.43$, $p = .15$] (see Figure 5). Therefore, contrary to prediction no relationship between nicotine withdrawal/craving severity and gender in the chronic pain sample was observed.

A test for homogeneity of variance for the hypothesis 3 analysis was assessed via the Levene test. This test showed a violation for the homogeneity assumption in the analysis between gender and nicotine withdrawal, but not in the analysis between gender and nicotine craving. When the homogeneity assumption is violated it is recommended that a lower p-value (e.g. $p < .01$) be used to detect significant difference (Maki, 2005). However, in the case of this analysis, p-values did not approach significance at traditional levels and therefore no attempts were made to correct this violation.

Hypothesis 4.

Hypothesis 4 predicted that among the chronic pain sample, nicotine withdrawal severity would be positively correlated with musculoskeletal pain, but unrelated to neuropathic pain. Withdrawal severity was assessed using the NWSC, musculoskeletal pain was assessed using the continuous pain subscale on the SF-MPQ-2, and neuropathic pain was assessed using the neuropathic pain subscale on the SF-MPQ-2. This hypothesis was tested via two linear regressions. Analyses did not reveal a significant relationships between nicotine withdrawal severity during deprivation and either average musculoskeletal pain [$R^2 = .04$, $F(1,12) = 0.50$, $p = .49$] or average neuropathic pain [$R^2 < .001$, $F(1,12) = 0.001$, $p = .98$]. Therefore, contrary to prediction no relationship between average musculoskeletal pain and nicotine withdrawal severity during deprivation was observed.

Statistical assumptions for hypothesis 4 regression analysis (i.e. linearity, homoscedasticity, and normality of errors) were assessed via reviews of appropriate graphs and plots (i.e. P-P plots, Q-Q plots, residual plots). No assumptions were violated in these analyses.

Hypothesis 5.

Hypothesis 5 predicted that, among the chronic pain group, an inverse relationship between average pain severity and readiness to quit smoking would be observed. Further, this hypothesis predicted that this relationship would be moderated by gender (men demonstrating a stronger relationship) and smoking consumption (heavier smokers demonstrating a stronger relationship). Readiness to change was assessed using the CL. This hypothesis was tested via 2 hierarchical linear regressions in which CL was entered as the dependent variable. In the first regression model gender and pain severity were entered in step 1, and a gender by pain severity interaction term was entered in step 2. Likewise, in the second regression model pack-years and pain severity were entered in step 1, and a pack-years by pain severity interaction term was entered in step 2. The normality of errors assumption was violated during the initial attempt to analyze this data using untransformed scores. Therefore, CL scores were transformed using a square-root transformation (Reich, 2006), which corrected this issue. The analysis of the first model did not reveal main effects of pain severity and gender [step 1; R^2 change=.13, $F(2,11) = 0.80$, $p = .46$], or an interaction between pain severity and gender [step 2; R^2 change=.04, $F(3,10) = 0.67$, $p = .59$]. Similarly, analysis of the second module did not reveal main effects of pain severity and pack-years [step 1; R^2 change=.20, $F(2,11) = 1.33$, $p = .30$], or an interaction between pain severity and pack years [step 2; R^2 change=.01, $F(3,10) = 0.85$, $p = .50$] (see Table 6).

Chapter IV

Discussion

The purpose of the present study was to investigate the relationship between chronic pain and several factors shown to be important to successful smoking cessation, specifically, nicotine withdrawal severity and stage of change. The discussion of this study is divided into three sections; a discussion of the effect of nicotine withdrawal on the experience of acute pain, and discussions on the effect of chronic pain on nicotine withdrawal/craving and stages of change. Within each section, current findings, as well as theoretical and clinical implications are discussed.

Nicotine Withdrawal and Acute Pain Experience

The current study found that nicotine deprivation did not have a statistically significant effect on acute musculoskeletal pain in men. However, it was observed that nicotine deprivation significantly decreased acute musculoskeletal pain among women. This finding is inconsistent with hypothesis 1, which was based on the existing literature suggesting that nicotine administration ameliorates acute laboratory induced pain, and that this ameliorative effect is more prominent among men than women. This contradictory finding has several important theoretical and clinical implications.

While it is unclear why women reported a significant decrease in pain severity following nicotine deprivation, there are some possible explanations. First, it is possible that pain medication use during deprivation may have masked elevations in pain resulting from nicotine deprivation. Further, it is possible that women received more pain relief from their medications compared to men; however, an analysis of pain medication use data during deprivation did not show gender differences in medication use or

effectiveness. Therefore, research which restricts or standardizes pain medication may be necessary to determine the effect of nicotine deprivation on pain experience.

Second, as stated earlier, there is considerable overlap in symptomatology between pain and nicotine withdrawal, including increased depression, difficulty relaxing (e.g. irritability), fatigue, and sleep disturbance (APA, 2000; Andersson, Ejlertsson & Leden, 1998). Given this overlap, it is possible that the overall increase in nicotine withdrawal severity and the saliency of the nicotine abstinence experience caused a reattribution of common symptoms as being part of a nicotine withdrawal experience, and not as part of the experience of pain. Further, there is some evidence in the literature suggesting that women experience greater withdrawal severity than men (Hatsukami, Skoog, Allen, & Bliss, 1995; Leventhal et al., 2007). Therefore, a reattribution of symptoms may have been more prominent in women, thus leading to the current finding.

Finally, it is possible that smoking and pain expectancies played a role in the current findings. For example, previous research has demonstrated that smoking outcome expectancies have an effect on the experience of nicotine withdrawal (e.g. Gottlieb, Killen, Marlatt, & Taylor, 1987; Wetter et al., 1994), and that expectancies regarding the relationship between cigarette smoking and the experience of pain influence smoking behavior (Ditre, Heckman, Butts, & Brandon, 2010). Therefore, it is possible that expectancies regarding the effect of smoking on pain affected the pain experience during deprivation. Further, since there are gender differences in smoking outcome expectancies (e.g. Weinberger, McKee, & George, 2010), there may also be gender differences in smoking and pain expectancies that led to the observed results. Further research is needed to elucidate the relationship between smoking and pain expectancies.

This finding (if replicated) also has clinical implications, as pain severity during nicotine deprivation may affect smoking cessation outcomes. Specifically, Ditre and colleagues (2008) demonstrated that pain induction can cue a smoking response. In the current study, women in the chronic pain group demonstrated decreased pain severity during deprivation. It is possible, therefore, that women who were abstinent from nicotine may experience fewer pain related smoking cues compared to their male counterparts, and that this difference may lead to gender differences in smoking cessation success in individuals with chronic pain. Future research should expand this finding by investigating pain related smoking cues among individuals who intend to quit smoking.

Chronic Pain and Nicotine Withdrawal

Hypotheses 2 though 4 predicted that those with chronic pain would experience greater nicotine withdrawal/craving severity (hypothesis 2), and that this relationship would be moderated by gender (hypothesis 3) and pain type (musculoskeletal versus neuropathic; hypothesis 4). However, contrary to these predictions the data showed no relationship between the experience of chronic pain and nicotine withdrawal/craving during deprivation. These results may represent a true lack of relationship between pain and nicotine withdrawal/craving. However, these results may also be the result of methodological limitations.

In addition to the general study limitations outlined below, these hypotheses may have also been affected by the following methodological limitations. First, 24-hours of deprivation is adequate to trigger withdrawal among most nicotine dependent individuals; however, the literature suggests that withdrawal may not peak until 1-2 weeks post cessation (Hughes, 2007) for some individuals. Therefore, it is possible that chronic pain

effects when an individual will experience the peak of withdrawal severity. Second, the majority of the pain group reported taking pain medications during the study. Given that there was a differential use of pain medications across groups, it is possible that the use of pain medication masked any differential effects on withdrawal. It is also possible that the pain group used pain medications to cope with withdrawal severity; however, this was not assessed. Third, all participants knew that they would resume smoking shortly after the deprivation session. Therefore, it is possible that the expectation of impending withdrawal relief may have ameliorated withdrawal severity, thus masking any expected findings. Finally, while participants were blind to the study hypotheses, no overt efforts were made to hide the true nature of the study. As the deprivation session contained few assessments, it was not hard to for participants to guess the purpose of the study. Therefore, these results may reflect demand characteristics.

Despite the null findings of this study, these data expand the literature by providing another demonstration of the independent nature of nicotine withdrawal and the experience of pain (Fertig, Pomerleau, & Sanders, 1986). Specifically, both groups demonstrated significant increases in nicotine withdrawal severity; however, there was no significant correlation between withdrawal severity and pain severity. Further, women in the chronic pain group showed significant decreases in musculoskeletal pain severity, while simultaneously demonstrating an increase in withdrawal severity. Therefore, despite overlap in symptomatology, and the potential permeability of symptoms across experiences, these processes appear to be interpreted and experienced independently.

Future research should retest these hypotheses and address the limitations noted above. Most importantly, future studies need to control for or standardize the differential

medication use across groups. This could be done by recruiting people who do not use pain medications, or by temporarily placing all pain group participants on an equivalent dose of narcotic pain medication. Additionally, future studies should use longer deprivation periods (e.g. 2 days to 1 week), and ecological momentary assessment strategies (EMA; repeated assessment of experiences in ones natural environment) to assess withdrawal/craving states in other settings. These strategies would provide a better understanding of the effect on chronic pain on nicotine withdrawal/craving trajectory and overall severity.

Clinically, the current findings suggest that it may not be necessary to differentially treat nicotine withdrawal/craving symptoms based on pain status. However, future research should test this assumption by including individuals who intend to quit smoking.

Chronic Pain and Readiness to Quit Smoking

An understanding of the relationship between readiness to quit smoking and chronic pain is important given its potential theoretical and clinical implications. Previous research has found no link among these constructs (Burkhalter et al., 2005; Hahn et al., 2006); however, the methods used in these studies were not optimal. The present study addressed some previous methodological concerns by investigating a sample of individuals with co-morbid chronic pain and nicotine dependence. However, consistent with previous literature, results from the current study did not reveal a relationship among smoking readiness to change and chronic pain severity. Interestingly, this study also found that there was no difference between the chronic pain and non-pain pain groups in

terms of readiness to quit smoking, and that most participants were identified as being in the contemplation stage of change based on the CL (Table 2).

While pain severity does not appear to be related to readiness to quit smoking, it is possible that it is related to other pain variables and associated symptoms. For example, a recent study found that the prevalence of major depressive disorder in former and current smokers was highest among those who have recently failed a quit attempt, followed by those who are contemplating quitting (Khaled, Bulloch, Exner, & Patten, 2009). Therefore, future research should investigate the relationship among pain and readiness to quit smoking by assessing the impact of a broader range of pain variables and related symptoms. Specifically, smoking cessation treatments might be improved through an investigation of the impact of pain duration, variability, frequency, and tolerance on readiness to quit smoking. Additionally, future research should investigate how common co-morbid conditions (e.g., depression, anxiety, physiological dysfunction) affect readiness to quit smoking.

Limitations

The findings from this study are likely affected by three general limitations: 1) low power, 2) sampling issues effecting generalizability, and 3) measurement re-norming. As stated in the methods section, the power analysis recommended a sample size of 24 participants per group (pain and no-pain) given a moderate effect size to reach a statistical power of .80 at the p=.05 level. This power analysis provided a conservative estimate of sample size, and the study was primarily powered to detect main effects between the groups. Unfortunately, despite the fact that all efforts were made to reach the goal of 48 total participants, we were unable to reach this goal due to recruitment

difficulties (see Appendix B). Therefore, it is likely that this study was underpowered to detect the hypothesized relationships, and these results may represent Type II errors.

Additional limitations of this study center on sampling issues. First, throughout data collection, this study had high attrition rates that were likely driven by concerns/discomfort regarding nicotine withdrawal, the significant time commitment required to complete assessments, and low reimbursement. Therefore, given the self-selecting nature of the sample, it is possible that our sample differs in important ways compared to the general population. Second, the modification of participant recruitment midway through the study likely influenced the results by broadening our sample, thus increasing between subjects random variance in the analyses. However, given that our strategies broadened participant recruitment beyond one specific primary care clinic, this change may have improved external validity. Finally, this study recruited current smokers who anticipated resuming smoking following the deprivation session. Therefore, the deprivation condition represents a “simulated quit attempt”, and not a “genuine quit attempt”. It is likely that the sample for this study differs in important ways compared to individuals making genuine quit attempts. Therefore, the generalizability of these results is limited, and the clinical implications listed in this document should be interpreted with caution.

The final limitation is that of re-norming, and stems from the creation of groups based on pre-existing pain status (pain or no-pain). Non-randomization is problematic for many reasons. Non-randomization is an issue in the current study because, as noted by Bartoschuk (2002) and others, there is no way to directly compare internal experiences; therefore, comparing sensory and emotional/psychological processes between groups that

are not presumed equal across important domains (e.g., the experience of pain) is problematic. In the context of the current study, it may not be reasonable to assume that a chronic pain participant's rating of "5" on a pain intensity scale is equivalent to a non-pain participant's rating of "5." Assuming that these ratings were the same could lead to confusing and inaccurate conclusions. Given this, we have taken a number of steps to address this problem. First, the two groups were not directly compared in terms of raw pain experience. Given that the groups, by definition, differ in their pain experience, these comparisons would be theoretically meaningless. Second, when cross group comparisons were made, individual change scores (post minus pre deprivations scores) were the comparison. Change score comparisons help account for initial differences between groups (i.e. reduces between group variability), and increases power by reducing within group variance in the analyses (Huck and McLean, 1975). Therefore, the variance caused by non-random group assignment is also reduced when using this method of data analysis.

Conclusions

While it is clear that a relationship between chronic pain and smoking exists, the nature of that relationship remains largely unknown. This study represents the first investigation examining the relationship between the experience of chronic pain and nicotine withdrawal/craving. The current study is also a replication of previous research examining the interaction between chronic pain and readiness to quit smoking. While the results of this study were likely affected by several limitations (e.g. limited power, measurement re-norming), two conclusions can be drawn. First, brief nicotine deprivation appears to decrease acute pain severity in women with chronic pain. If this finding

withstands replication, it will have significant theoretical and clinical implications. Second, consistent with previous literature, this study does not support a relationship between chronic pain severity and readiness to quit smoking. However, pervious literature suggests that readiness to quit smoking is related to factors often co-occurring with pain. Therefore, research investigating the relationships among chronic pain, readiness to quit smoking, and common co-morbid concerns (e.g. depression) is warranted. In conclusion, chronic pain and smoking represent significant health concerns, and our work in elucidating the relationship between the two is far from complete.

Table 1: Sample demographics

Variable	Total Sample	Chronic Pain Group	Non-Pain Group
Age: Mean(SD)	46.76 (11.68)	47.21 (10.42)	45.86 (14.78)
Years of Education: Mean(SD)	12.28 (2.39)	12.07 (2.67)	12.71 (1.79)
Sex:			
Male	14 (66.7%)	8 (57.1%)	6 (85.7%)
Female	7 (33.3%)	6 (42.9%)	1 (14.3%)
Ethnicity:			
African American	1 (4.8%)	1 (7.1%)	0 (---)
Caucasian	16 (76.2%)	10 (71.4%)	6 (85.7%)
Hispanic	2 (9.5%)	2 (14.3%)	0 (---)
Native American	1 (4.8%)	1 (7.1%)	0 (---)
Other	1 (4.8%)	0 (---)	1 (14.3%)
Marital Status:			
Married	6 (28.6%)	4 (28.6%)	2 (28.6%)
Single	2 (9.5%)	0 (---)	2 (28.6%)
Widowed	3 (14.3%)	2 (14.3%)	1 (14.3%)
Dating	1 (4.8%)	1 (7.1%)	0 (---)
Cohabitating	1 (4.8%)	1 (7.1%)	0 (---)
Divorced	7 (33.3%)	5 (35.7%)	2 (28.6%)
Engaged	1 (4.8%)	1 (7.1%)	0 (---)

Note. Interval data analyzed via ANOVA, categorical Data analyzed via Chi-square analysis.
**p< .05. **p<.01*

Table 2: Smoking and Pain Characteristics

Variable	Total Sample	Chronic Pain Group	Non-Pain Group
Cigarette Consumption: Mean(SD)	23.05 (8.87)	23.43 (6.44)	22.29 (13.10)
Years Smoking: Mean(SD)	17.89 (13.79)	17.57 (12.71)	18.53 (16.84)
FTND Score: Mean(SD)	7.05 (1.36)	7.07 (1.27)	7.00 (1.63)
Intake Expired CO Level: Mean(SD)	23.19 (7.96)	22.86 (9.19)	23.86 (5.27)
Contemplation Ladder: Mean(SD)	7.10 (3.15)	7.43 (3.03)	6.43 (3.51)
Baseline SF-MPQ-2 Scores:			
Total	55.38 (54.15)	80.79** (49.17)	4.57** (4.08)
Continuous	18.00 (17.40)	26.50** (15.20)	1.00** (1.73)
Intermittent	15.10 (17.58)	22.64** (17.08)	0.00** (0.00)
Neuropathic	15.05 (15.74)	22.00** (14.97)	1.14** (1.57)
Affective	2.68 (10.65)	3.00 (14.57)	2.43 (2.50)
Pain Duration in Years: Mean(SD)	----	7.86 (7.93)	----

Note. Interval data analyzed via ANOVA.
**p< .05. **p<.01*

Table 3: Mental Health Characteristics

Variable	Total Sample	Chronic Pain Group	Non-Pain Group
CES-D Score: Mean(SD)	31.14 (9.15)	32.64 (9.59)	28.14 (7.99)
Mental Health Dx: Freq.			
Major Depression	9 (42.9%)	5 (35.7%)	4 (57.1%)
Anxiety disorders	3 (14.3%)	1 (7.1%)	2 (28.6%)
MINI Interview: Freq.			
ETOH Dependence	2 (9.5%)	1 (7.1%)	1 (14.3%)
Drug Dependence	0 (---)	0 (---)	0 (---)
Pain Medication Use: Freq.	14 (66.67%)	13** (92.8%)	1** (14.3%)
Current effectiveness of pain medications	----	5.78^{+} (2.69)	----
Urine Analysis: Freq.			
THC	3 (14.2%)	3 (21.4%)	0 (---)
Amph	2 (9.5%)	1 (7.1%)	1 (14.3%)
Opiods	6 (28.6%)	6 (42.9%)	0 (---)
Benzo	5 (23.8%)	3 (21.4%)	2 (28.6%)
Cocaine	0 (---)	0 (---)	0 (---)
Quality of Life Score:	40.46 (17.11)	41.55 (17.99)	38.26 (16.34)
Medical Comorbidity: Mean (SD)	6.69 (6.52)	7.88 (7.12)	4.80 (5.63)

Note. Interval data analyzed via ANOVA, categorical Data analyzed via Chi-square analysis.
**p< .05. **p<.01*
+There were no gender differences in the reported effectiveness of pain medications during deprivation

Table 4: PAI- Validity and Clinical Scales

Variable	Total Sample	Chronic Pain Group	Non-Pain Group
Validity Scales:			
Mean(SD)			
ICN	52.38 (11.39)	53.53 (12.15)	50.11 (10.18)
INF	48.73 (7.42)	50.21 (7.39)	45.76 (7.05)
NIM	60.84 (14.56)	62.79 (16.43)	56.97 (9.77)
PIM	45.36 (10.67)	48.20 (10.11)	39.68 (10.07)
Clinical Scales:			
Mean(SD)			
SOM	72.65 (13.86)	78.35**(12.98)	61.26**(6.90)
ANX	62.50 (13.20)	63.15 (12.64)	61.20 (15.22)
ARD	61.24 (12.99)	61.30 (15.07)	61.12 (8.39)
DEP	65.96 (12.93)	67.73 (14.16)	62.43 (10.04)
MAN	54.22 (12.21)	52.16 (11.38)	58.36 (13.67)
PAR	58.41 (14.13)	56.22 (13.27)	62.80 (15.83)
SCZ	61.20 (14.39)	61.47 (16.16)	60.65 (11.13)
BOR	62.21 (12.14)	60.90 (13.52)	64.83 (9.12)
ANT	58.66 (12.94)	54.37* (9.65)	67.23* (15.10)
ALC	54.28 (14.69)	49.41* (10.08)	64.03* (18.25)
DRG	58.69 (13.66)	57.98 (14.99)	60.13 (11.48)

Note. Interval data analyzed via ANOVA.
**p< .05. **p<.01*

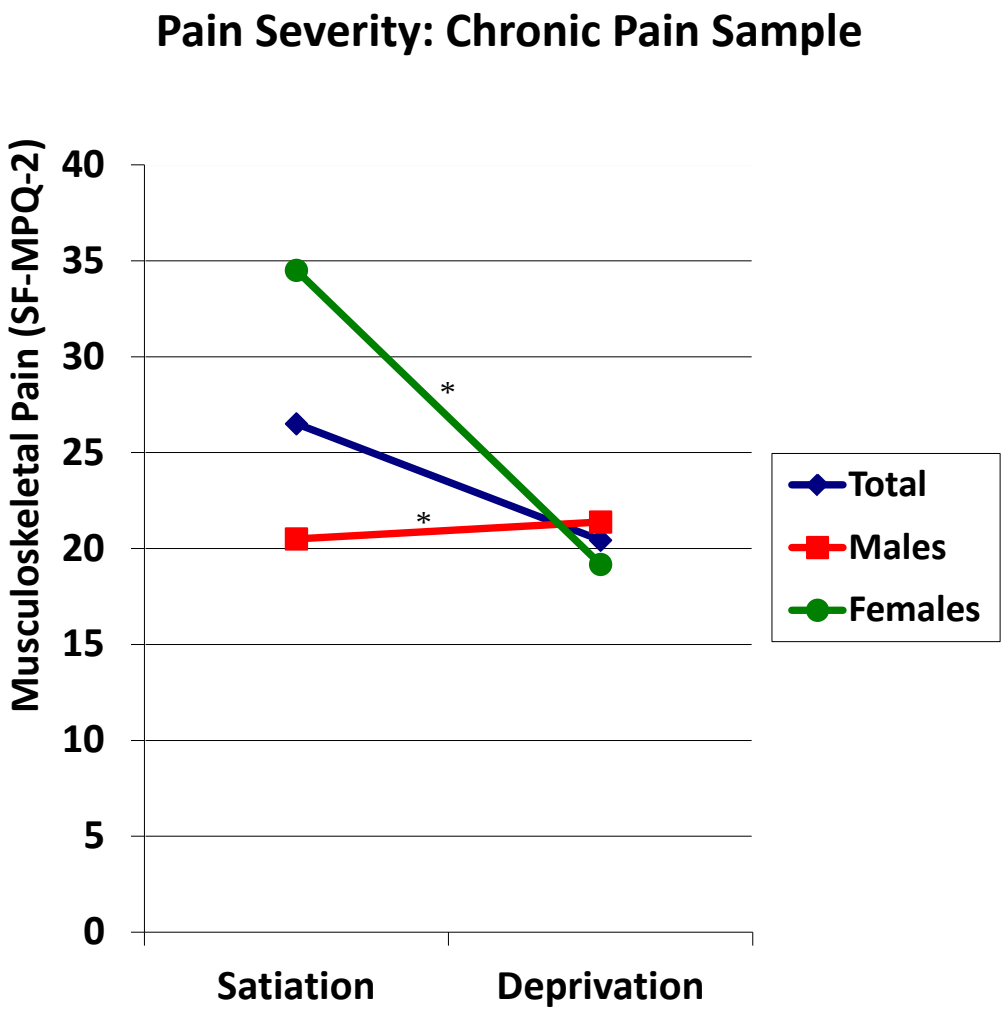
Table 5:PAI- Treatment and Interpersonal Scales

Variable	Total Sample	Chronic Pain Group	Non-Pain Group
Treatment Scales:			
Mean(SD)			
AGG	52.54 (9.75)	50.90 (9.72)	55.82 (9.67)
SUI	56.48 (14.37)	53.69 (11.96)	62.06 (17.99)
STR	61.79 (13.02)	63.61 (14.13)	58.15 (10.45)
NON	56.37 (13.70)	54.74 (15.36)	59.61 (9.81)
RXR	44.37 (10.65)	46.06 (10.31)	40.99 (11.30)
Interpersonal Scales:			
Mean(SD)			
DOM	46.03 (8.53)	46.24 (7.32)	45.60 (11.24)
WRM	44.83 (14.91)	45.09 (15.77)	44.33 (14.20)

Note. Interval data analyzed via ANOVA.
**p< .05. **p<.01*

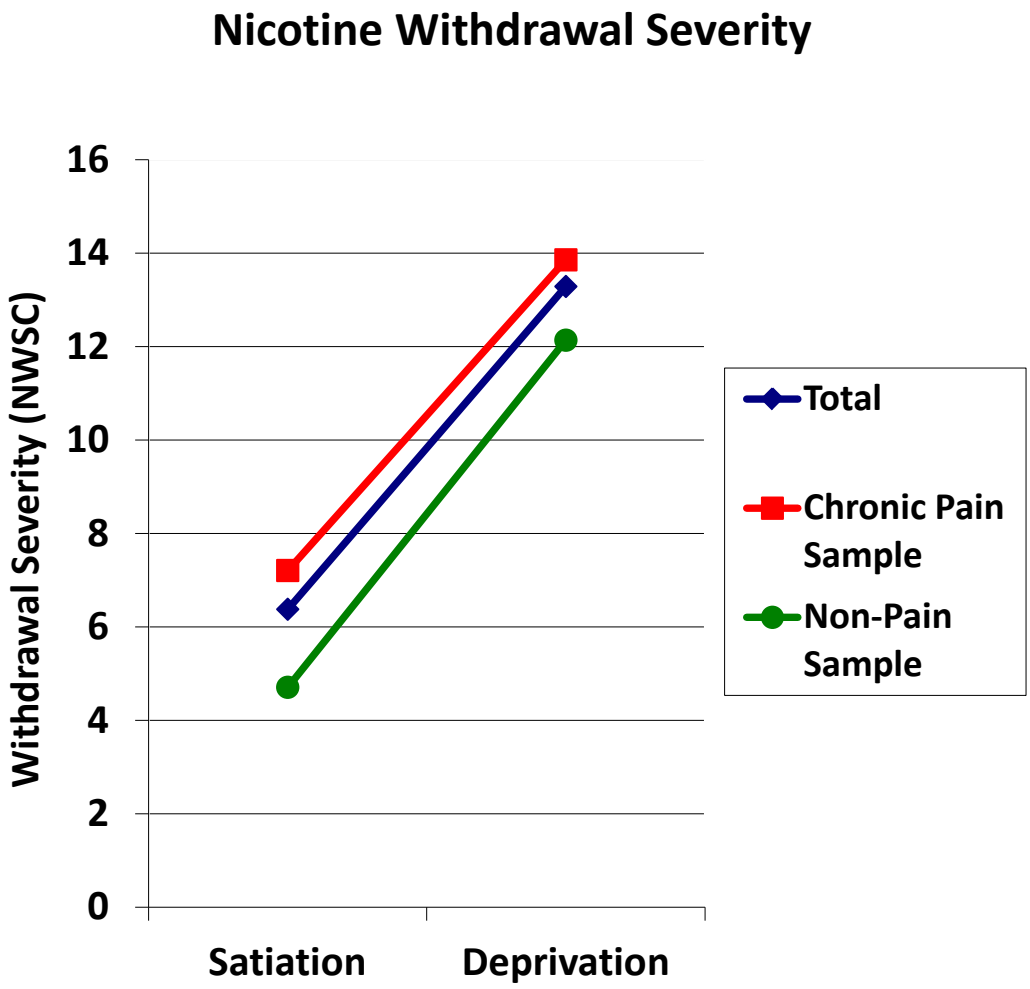
Table 6: Regression Analysis: Predicting Smoking Readiness to Change (CL)

Regression Model	R^2 Change	β	t	p
Pain and Gender				
Step 1	.13			
Pain Severity		-.02	-.07	.95
Gender		-.37	-1.16	.27
Step 2	.04			
Pain Severity		.16	.16	.70
Gender		-.12	-.12	.81
Pain X Gender		-.31	-.31	.50
Pain and Pack-Years				
Step 1	.20			
Pain Severity		.02	.07	.95
Pack-Years		-.44	-1.54	.15
Step 2	.01			
Pain Severity		.09	.24	.82
Pack-Years		-.34	-.77	.46
Pain X Pack-Years		-.14	-.32	.76



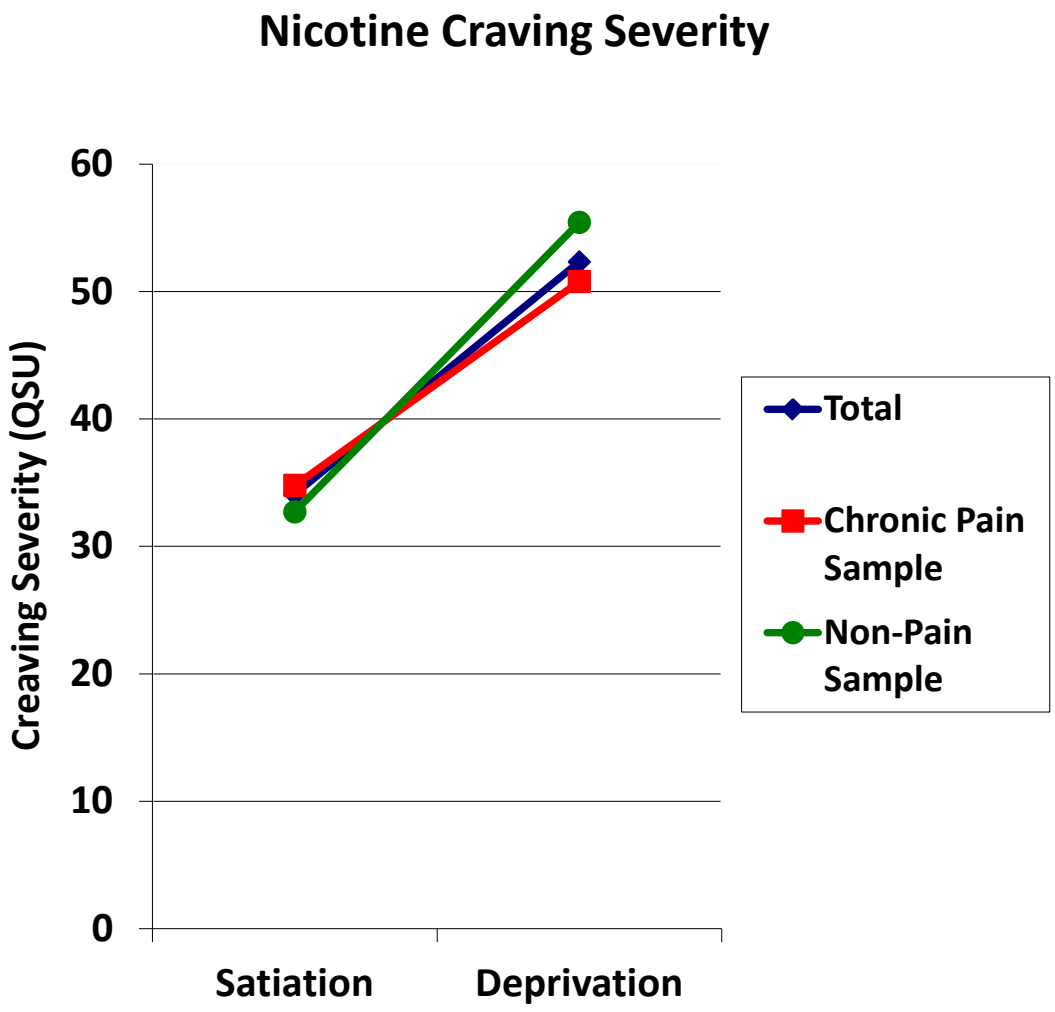
*p<.05

Figure 1: Chronic Pain Sample- Musculoskeletal Pain Levels During Deprivation



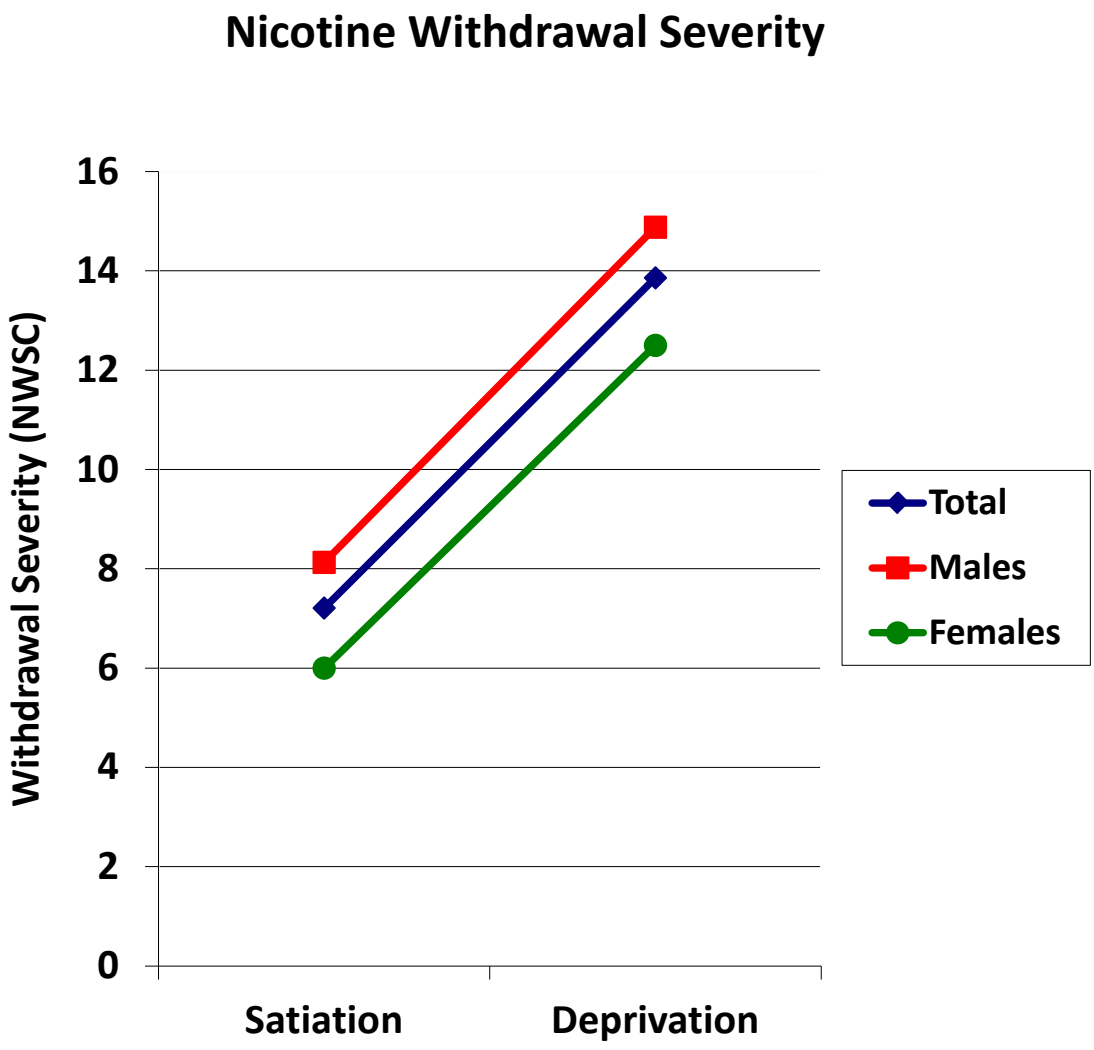
*p<.05

Figure 2: Total Sample- Nicotine Withdrawal Severity



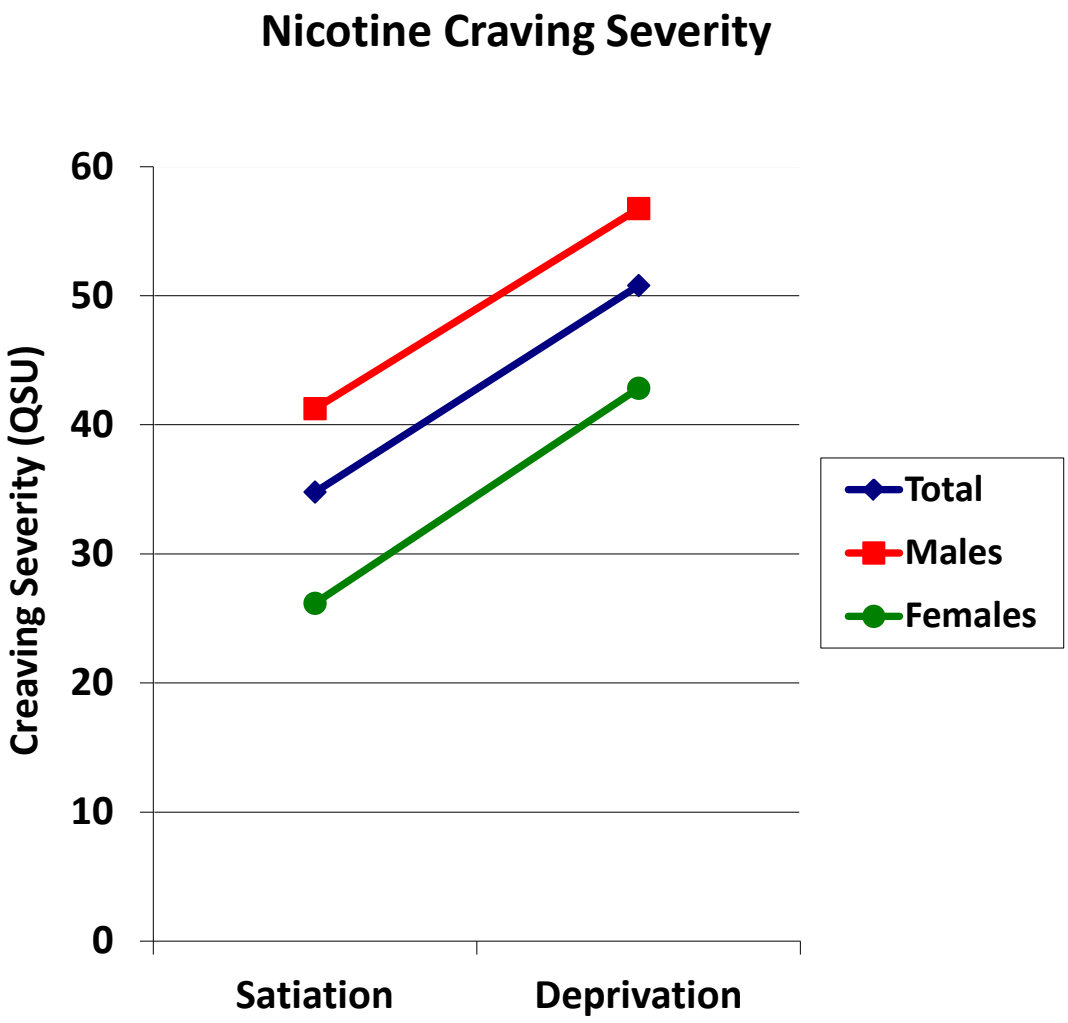
$p<.05$

Figure 3: Total Sample- Nicotine Craving Severity



$p<.05$

Figure 4: Chronic-Pain Sample- Nicotine Withdrawal Severity



**p<.05*

Figure 5: Chronic-Pain Sample- Nicotine Craving Severity

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Appendix A:

Extended Literature Review

Introduction

Smoking and chronic pain are independently associated with serious health concerns (National Institute on Drug Abuse [NIDA], 2009;Gran, 2003). For example, smoking is the leading preventable cause of death in the United States, responsible for 440,000 deaths per year (NIDA, 2009). Additionally, chronic pain is associated with considerable adverse health effects (Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Gran, 2003). While the independent health consequences of these problems are disconcerting, the finding that smoking and chronic pain often co-occur highlights that this co-morbid population is at increased risk for morbidity and mortality. The study proposed above aims to elucidate the relationship between chronic pain and smoking with an eye towards investigating several factors known to influence smoking cessation success, including nicotine withdrawal experience, readiness to change, and gender. The literature review that follows will lay the empirical foundation for this study.

This literature review is divided into three sections. In section 1, several topics pertinent to smoking and nicotine will be reviewed. These topics will include brief overviews of the history of smoking in the U.S., nicotine dependence criteria (as defined by the DSM-IV-TR), nicotine withdrawal symptoms, moderators of withdrawal, the effects of gender on withdrawal, and readiness to change. Section 2 will provide a brief overview of chronic pain including pain theories, pain experience, and key physiological and psychological pain factors. Finally, section 3 will review the literature linking pain experience and smoking/nicotine consumption. Specifically, section 3 topics include a

discussion of the effects of smoking on pain, chronic pain and readiness to change, and chronic pain and nicotine withdrawal. Section 3 will also highlight gaps in the literature laying the foundation for the proposed study.

Section 1: General Overview of Nicotine

Nicotine Use: A brief historical perspective

As stated above, smoking is the single leading preventable cause of death in the U.S. (NIDA, 2009). The first nationally recognized evidence linking cigarette smoking to increased morbidity and mortality was published by the U.S. Department of Health, Education, and Welfare in 1964 (U.S. Department of Health, Education, and Welfare [US DHEW], 1964). After a review of approximately 7,000 empirical studies, this report found that smoking was linked to lung and laryngeal cancers in men, and was likely a cause for lung cancer in woman. Since this publication, research has linked cigarette smoking to a variety of health problems including various cancers (e.g. lung and leukemia), cardiovascular disease, heart attacks, stroke, bronchitis, emphysema, and pneumonia (NIDA, 2009; Wadland & Ferenchick, 2004). Additionally, maternal smoking and second-hand smoke have been linked to increased still-birth rates, miscarriage, low birth weight, sudden infant death syndrome, learning disorders, and behavior problems (NIDA, 2009). Due to these and other findings, the U.S. federal government has passed a series of laws and regulations restricting the packaging and advertisement of cigarettes. Early federal tobacco regulation included the Federal Cigarette Labeling and Advertising Act of 1965 and the Public Health Cigarette Smoking Act of 1969. These laws banned all cigarette advertisement on the television and radio, and required warnings to appear on

all cigarette packages and printed advertisements outlining the deleterious health effects of smoking (U.S. Department of Health and Human Services [US DHHS], 1989).

The increased knowledge regarding the health effects of smoking, changes in public attitudes towards smoking, and strong federal tobacco regulation have lead to significant decreases in smoking prevalence (US DHHS, 1989). However, the public health impact of smoking remains significant, and the most likely outcome of any given cessation attempt remains relapse (Piasecki, 2006). Further, it has been suggested that as smoking prevalence in the U.S. decreases, those who continue to smoke are less likely to be able to quit due to nicotine dependence (Hughes, Goldstein, Hurt, & Shiffman, 1999). Therefore, research which focuses on those factors which put individuals at an increased risk for failed smoking cessation and health complications is warranted.

Nicotine Dependence

The DSM-IV-TR (American Psychiatric Association [APA], 2000) defines three nicotine related disorders including Nicotine Withdrawal (292.0), Nicotine Dependence (305.1), and Nicotine-Related Disorder Not Otherwise Specified (292.9) (page 264). This section includes a brief description of Nicotine Dependence criteria. An in-depth discussion of nicotine withdrawal is provided in the following section.

Nicotine dependence is defined via the same criteria as other substances. These criteria include: 1) Tolerance defined by either a need to increase substance use to gain similar effects or diminished effect with continued use of the same amount, 2) Withdrawal as defined be either the characteristic (nicotine) withdrawal syndrome or a need to take a similar substance to elevate withdrawal symptoms, 3) Substance is taken in greater quantities or over a longer period of time than planned, 4) A desire, or previous

unsuccessful attempts, to cut down or control use, 5) Significant time spent obtaining the drug, using the drug, and recovering from drug use, 6) Impairment in social, occupational, or recreational activities due to substance use, and 7) Continued use despite knowledge of having a persistent/recurrent physical or psychological problem which has likely been caused/exacerbated by substance use (APA, 2000). Additionally, the standard substance dependence specifiers apply to nicotine (i.e. remission specifiers and physiological dependence specifiers) (APA, 2000). These general dependence criteria provide a guideline for diagnosis; however, given that substances differ as to general use patterns, pharmacological profile, and legal implications, special considerations must be made when diagnosing specific substance dependence disorders.

Given the unique characteristics of nicotine, several considerations must be made when making the nicotine dependence diagnosis (APA, 2000). First, tolerance of nicotine is manifested by a “more intense effect” with the first use of the day, as compared to any other use. Also, tolerance is evidenced by a lack of dizziness or nausea despite repeated use (criterion 1). Second, nicotine users often use when they wake up in the morning, or following extended periods when use is restricted (e.g. during a movie), to alleviate withdrawal symptoms (criterion 2). Third, individuals who use nicotine containing products frequently use their supply faster than intended (criterion 3). Fourth, despite the fact that the vast majority of smokers desire to quite, the single most likely outcome of any quit attempt is relapse (criterion 4). Fifth, spending a great deal of time using nicotine is best demonstrated by chain-smoking. Also, because nicotine products are legal, spending considerable time obtaining these products is unlikely (criterion 5). Sixth, role impairment (impairment in social, occupational, or recreational activities) is manifested

when someone abstains from one of these activities because nicotine use is prohibited (criterion 6). Finally, nicotine use has been associated with considerable health consequences; therefore, the 7th criterion (i.e. continued use despite associated health/psychological problems) is especially important to the diagnosis (APA, 2000).

Nicotine Withdrawal

Research has identified nicotine withdrawal as an important factor in predicting smoking cessation success. Specifically, nicotine withdrawal experience has been linked to latency of smoking relapse, with individuals who experience more severe withdrawal demonstrating greater difficulty abstaining from cigarettes (Piasecki, Fiore, & Baker, 1998). Therefore, studies which elucidate the factors that influence nicotine withdrawal experience are important.

While several definitions of withdrawal symptoms have been proposed, one of the best definitions comes from Hughes (2007) who defined a *withdrawal symptom* is an "abstinence effect with time-limited increase or decrease" (page 128), suggesting that withdrawal symptoms are transient experiences. He goes on to contrast withdrawal symptoms with *off-set effects*, which he defined as "abstinence effect[s] with unidirectional change" (page 128), suggesting that that they are permanent as long as abstinence is maintained. These unidirectional changes can also include preexisting conditions (e.g. depression) masked by substance use (Shiffman, West, & Gilbert, 2004). The DSM-IV-TR (APA, 2000) defines nicotine withdrawal as including four (or more) of the following symptoms: 1) dysphonic or depressed mood, 2) insomnia, 3) irritability, frustration, or anger, 4) anxiety, 5) difficulty concentrating, 6) restlessness, 7) decreased heart rate, and 8) increased appetite or weight gain. Each of these abstinence effects has

been consistently documented in the literature as occurring following smoking cessation. However, there has been some debate as to whether some of these abstinence effects should be included in the DSM-IV-TR as true withdrawal symptoms.

The discussion that follows provides an overview of smoking abstinence effects commonly cited in the literature, and includes both withdrawal symptoms and off-set effects. This section includes two sub-sections based on inclusion in the DSM-IV-TR (i.e. those included in the DSM-IV-TR criteria, and those not included). Each abstinence effect reviewed will include a discussion of the relevant research for that effect, as well as a brief discussion of time course. Additionally, each overview will conclude with a brief discussion regarding its inclusion in the DSM-IV-TR as a withdrawal symptom, based on the Hughes (2007) definition. Finally, this section will conclude with a general discussion of the time course of nicotine withdrawal.

DSM-IV-TR defined nicotine withdrawal symptoms.

Dysphonic or Depressed Mood: Negative affect (NA), which induces depressive and dysphonic moods, is cited as a common substance offset effect, as it is found in several substance withdrawal profiles including nicotine (Hughes, Higgins, & Bickel, 1994; Shiffman et al., 2004). Generally, studies using self-report measures have found that NA tends to increase during periods of abstinence. This finding has been generally consistent across assessment methodologies. For example, NA has been shown to increase following smoking cessation in studies utilizing standard single and repeated measurement designs (Hughes, 2007), ecological momentary assessment paradigms (EMA) (McCarthy, Piasecki, Fiore, & Baker, 2006; Shiffman et al., 2006), and mood modulation procedures (Dawkins, Acaster, & Powell, 2007). These studies generally

suggest that NA significantly increases on the quit date and remains elevated for 6 days to 3 weeks. Further, self-report studies suggest that approximately 20% of recent quitters report experiencing low mood (C. S. Pomerleau, Marks, & Pomerleau, 2000).

While the majority of studies investigating NA as a withdrawal effect have relied on self-report assessment methodologies, self-report methodologies fall subject to a number of well documented biases. Therefore, many researchers have begun to expand their assessment strategies to include objective assessment paradigms which can avoid these biases. One objective measurement technique commonly utilized in the nicotine literature uses the human eye-blink startle response as a physiological proxy for NA. Specifically, as part of the startle paradigm, participants are administered an aversive stimuli (e.g. loud white noise), and their startle response is measured via the eye blink reflex (Postma, Kumari, Sharma, Hines, & Gray, 2001). This response is considered a physiological analogue to NA as it can be modulated by emotionally provocative images (Cinciripini et al., 2006). In general, this body of research suggests that deprived smokers experience increased NA following smoking cessation as measured by delayed habituation to aversive stimuli (lower pre-pulse inhibition), exaggerated negatively modulated startle response, and prolonged extinction curves following signal-stimuli pairing (Cinciripini et al., 2006; Hogle & Curtin, 2006; Kumari & Gray, 1999). While the bulk of the objective assessment literature supports the notion that NA is a reliable abstinence effect, these paradigms are new and so not surprisingly inconsistent findings exist (e.g. Cinciripini et al., 2006; Piper & Curtin, 2006). However, the bulk of the rigorous self-report and objective measurement studies have linked nicotine abstinence to

depressed and dysphonic mood, suggesting that it is a reliable abstinence effect (Hughes, 2007).

Research on the time course of abstinence induced NA evidences a biphasic trajectory, suggesting that it is a true nicotine withdrawal symptom (Hughes, 2007). However, despite the consistency of which NA is document following nicotine cessation, there is considerable variability in reported time courses. For example, Shiffman and colleagues (2006) found that NA symptoms abated within 7 days post abstinence, using an EMA paradigm. However, other studies have found that NA remains elevated for 3 or more weeks after cessation (McCarthy et al., 2006; Piasecki et al., 2000). Therefore, further research is needed to provide clarification on the factors which influence the time course of NA (Hughes, 2007).

Insomnia: Sleep disturbance is a commonly cited symptom of nicotine withdrawal, as well as many other substances (Hughes et al., 1994; Shiffman et al., 2004). Studies utilizing self-report measures have highlighted a number of findings. Specifically, decreased sleep quality and quantity are common during smoking abstinence (Shiffman et al., 2004). Studies using objective sleep measures have found similar results, and have demonstrated that nicotine abstinence can lead to sleep fragmentation (sleep disturbances) including nocturnal arousal (increased EEG activity), nocturnal awakenings, and increased sleep stage shifts (Hughes, 2007; Wetter et al., 2000; Wetter, Fiore, Baker, & Young, 1995; Wetter et al., 1999). These types of sleep disturbances (i.e. nocturnal awakenings) have been reported in approximately 39% of recent quitters, and appear to last between three and five days post cessation (Hughes, 1992; Shiffman et al., 2006).

Research on the time course of insomnia and sleep changes post cessation evidences a biphasic trajectory, with studies utilizing both objective and self-report measures consistently demonstrating that it increases within one day of abstinence, and generally remits within five days. Therefore, insomnia appears to be a true withdrawal symptom, as defined by Hughes (2007).

Irritability, Frustration, and Anger: Irritability is another DSM-IV-TR (2000) defined nicotine withdrawal symptom that is common to many substance withdrawal profiles (Hughes et al., 1994). Research on irritability, frustration, and anger have consistently shown that these symptoms fluctuate following smoking cessation (Gilbert et al., 1998; Gilbert et al., 2002; Hughes, 1992, 2007; Jorenby, Hatsukami, Smith, & Fiore, 1996; Shiffman et al., 2004). Specifically, these symptoms appear to peak in intensity within 7 days following a quit attempt (Gilbert et al., 2002; Hughes, 1992, 2007), and generally remit within two weeks to a month (Gilbert et al., 2002). Given that these symptoms consistently demonstrate a biphasic trajectory, they appear to be a true nicotine withdrawal symptom.

Anxiety: Anxiety, like depression, has been consistently shown to increase following nicotine abstinence (Hughes, 1992, 2007; Jorenby et al., 1996; Shiffman et al., 2004; Zvolensky et al., 2005). Further, while research has demonstrated that general anxiety increases, it has also demonstrated that withdrawal may increase specific anxiety processes, including panic sensitivity. This findings suggest that nicotine withdrawal may make some individuals hyper-vigilant regarding physiological arousal, predisposing them to panic symptoms (Zvolensky et al., 2005). The majority of findings have demonstrated that abstinence related anxiety is biphasic, peaking within 1 to 3 days and remitting after

approximately 2 weeks post cessation (Hughes, 2007; Jorenby et al., 1996). The biphasic trajectory of this effect suggests that it is a true nicotine withdrawal symptom.

Difficulty Concentrating: Difficulty concentrating has been consistently demonstrated in the literature, and is common to many substance use withdrawal profiles (Hughes, 1992, 2007; Shiffman et al., 2004). Studies relying on self-report measures of concentration have generally demonstrated that concentration decreases following smoking abstinence (Gilbert et al., 2002; Jorenby et al., 1996). Further, studies that have used objective measurements (e.g. neuropsychological batteries) indicate that nicotine abstinence negatively effects mathematical reasoning (al' Absi, Amunrud, & Wittmers, 2002; Shiffman et al., 2006; Shiffman, Paty, Gnys, Kassel, & Elash, 1995), visuospatial memory (Jacobsen, Slotkin, Westerveld, Mencl, & Pugh, 2006), working and verbal memory (Jacobsen et al., 2005), and delayed reward tolerance. Further, research demonstrates that difficulty concentrating peaks within 2 days of abstinence, and remits between 1 and 4 weeks (Hughes, 1992, 2007). Given the consistency with which concentration difficulties have been identified in the literature following nicotine abstinence, and the evidenced biphasic symptom trajectory, it appears to be valid nicotine withdrawal symptom.

Restlessness: Restlessness has been consistently documented in the literature as a nicotine abstinence effect (Gritz, Carr, & Marcus, 1991; Hughes, 1992, 2007; Hughes et al., 1994; Shiffman et al., 2004). Specifically, studies utilizing self-report measurements of restlessness have constantly documented that restlessness increases following cessation (Gritz et al., 1991; Hughes, 1992; Jorenby et al., 1996; Shiffman et al., 2006), peaking within 1 to 3 days post abstinence, and abating within 4 weeks (Hughes, 2007;

Shiffman et al., 2004). Given the biphasic nature of restlessness, it is likely that it is a true withdrawal symptom. However, it should be noted that it is unclear if restlessness is conceptually different from irritability and impatience, given the moderate correlations observed among these constructs (Hughes, 2007). Therefore, a better operational definition may be warranted.

Decreased Heart Rate: Decreased heart rate has been one of the most reliability demonstrated nicotine abstinence effects (Gilbert et al., 1999; Hughes, 1992). This is unsurprising, give that nicotine is a stimulant which increases heart rate (Smith, Tong, & Leigh, 1977). Further, the absence of nicotine causes a uniphasic decrease in heart rate (e.g. decreased heart rate is maintained as long as abstinence is maintained). Therefore, based on Hughes (2007) definition, decreased heart rate appears to be an off-set effect and not a true withdrawal symptom (Hughes, 2007; Shiffman et al., 2004). Given this, it has been proposed that heart rate changes should not be included as part of the nicotine withdrawal profile (Shiffman et al., 2004), and inclusion as a DSM-IV-TR nicotine withdrawal symptom is questionable.

Increased Appetite and Weight Gain: Increased appetite and weight gain are common in abstinent smokers (Hughes, 1992; Hughes et al., 1994, Shiffman et al., 2004). Specifically, approximately 10% of abstainers report excessive hunger, and 25% report eating more than usual after 12 months of abstinence (Gritz et al., 1991). However, appetite and weight gain do not to return to pre-abstinence levels, suggesting that they have a uniphasic trajectory. Therefore, based on the Hughes (2007) definition these symptoms should be considered off-set effects and not withdrawal symptoms (Shiffman et al., 2004), and inclusion as a DSM-IV-TR nicotine withdrawal symptom is

questionable. However, as weight gain is aversive, and weight concerns are commonly cited barriers to smoking cessation, there is clinical and research utility in measuring these variables in abstaining smokers (Shiffman et al., 2004).

Withdrawal effects not included in the DSM-IV-TR.

Nicotine Craving: Nicotine craving is commonly reported during nicotine abstinence (Shiffman et al., 2004). Specifically, craving has been reported in approximately 76% of first day abstainers, and 17% of those abstinent after one year (Gritz et al., 1991). Research has consistently demonstrated that craving peaks within 1 to 2 days post cessation (Jorenby et al., 1996; McCarthy et al., 2006; VanderVeen, Cohen, Trotter, & Collins, 2008; Zinser, Baker, Sherman, & Cannon, 1992). However, the resolution timeline for craving is less clear, with available estimates ranging from 3 days to over three weeks (McCarthy et al., 2006). As craving during nicotine abstinence is biphasic, (Gritz et al., 1991; Jorenby et al., 1996), it should be considered a nicotine withdrawal symptom. However, it is important to note there is disagreement on an operational definition of craving and thus considerable heterogeneity in how it is measured (Sayette et al., 2000); therefore, research should focus to resolve these important discrepancies.

Constipation: One study to date has identified constipation as a potential withdrawal effect. Specifically, Hajek, Gillision, and McRobbie (2003) found that approximately 17% of abstinent smokers reported some level of constipation, with approximately 9% reporting severe symptoms. In their study, they found that constipation peaked at 2 weeks post cessation, and failed to remit during the 4 week observation period. However, as little is known about constipation following nicotine abstinence, it is

not possible to determine at this time if constipation should be a withdrawal effect or off-set effect. Further research is warranted.

Fatigue and Arousal: There is a lack of clear evidence supporting the inclusion of fatigue and/or arousal changes as symptoms of nicotine withdrawal. Specifically, several well designed studies have failed to find constant links between fatigue, arousal, and nicotine abstinence (Hughes, 2007). This issue is likely partially driven by poor operational definitions of both constructs, and considerable overlap between these constructs and other withdrawal effects. For example, it is unclear how arousal is different from fatigue. Specifically, Shiffman and colleagues (1995) measured arousal using a multi-item self report measure which assessed alertness, sharpness, drowsiness, difficulty concentrating, and feeling "spacey." It could be argued that their measure assessed fatigue as much as arousal. Further, fatigue may be better accounted for by other withdrawal symptoms, including fragmented sleep, restlessness, or depression. Therefore, given a lack of consistent support for fatigue and arousal as a withdrawal symptoms (Hughes, 2007), the fact that they could be the result of other withdrawal effects, and that there is a lack of adequate operational definitions, it is unlikely that these symptoms represent valid components of nicotine withdrawal.

Impatience: Approximately 38% of first day nicotine abstainers, and 47% of 1 week nicotine abstainers report experiencing some increased impatience (Gritz et al., 1991). This finding has been relatively consistent, despite the fact that few studies have investigated the effects of nicotine abstinence and impatience. This abstinence effect appears to peak within the first few days of cessation, and typically remits following 3 weeks or more (Gritz et al., 1991; Hughes, 2007; Jorenby et al., 1996). However, the

literature lacks a clear operational definition of impatience, as there is considerable definitional overlap between impatience and restlessness, irritability, and frustration. Specifically, Hughes (2007) stated that impatience can be defined as "(a) problems waiting, (b) problems enduring *irritation* or being annoyed, and (c) *restlessness*" (p. 320). Therefore, further research is needed to determine if impatience should be considered separate from irritability and restlessness (Hughes, 2007).

General Discussion of Time Course

The ability to estimate the time course of nicotine withdrawal has significant clinical and research implications, and several researchers have attempted to provide such estimates. Currently, one of the best nicotine withdrawal time course estimates comes from Hughes (2007), who suggested that nicotine withdrawal peaks within 1-2 weeks, and remits following 3 to 4 weeks of cessation. However, there are several significant problems with aggregate level estimates (like the one provide by Hughes, 2007) which limited their utility. Specifically, the literature evidences considerable inter and intra-symptom time course heterogeneity. For example, some symptoms appear to return to baseline within 1 week post cessation while others fail to remit within 3 weeks. Also, studies measuring the same withdrawal symptom show considerable differences in the time it takes for those symptoms to resolve (e.g. NA: Gilbert et al., 1999; Jorenby et al., 1996). Therefore, more powerful analytical tools are needed to better understand nicotine withdrawal time course.

Moderators of Nicotine Withdrawal

As noted above, there is considerable variability in the time course and severity of nicotine withdrawal symptoms. Therefore, a clear understanding of moderators, which

effect the presentation of nicotine withdrawal, is important. In the section that follows, a discussion of selected moderators of nicotine withdrawal is presented, including a brief review of the relevant literature for each.

Depression, NA, and low mood.

Depression has been consistently identified as an important moderator of nicotine withdrawal, and has subsequently received significant empirical attention. Specifically, increased NA or a history of depression have been associated with elevated nicotine withdrawal severity (Madden et al., 1997; Niaura et al., 1999; Strong, Kahler, Ramsey, Abrantes, & Brown, 2004), including elevated depressive symptoms (Covey, Glassman, & Stetner, 1990; Niaura et al., 1999; C. S. Pomerleau et al., 2000). Further, a history of depression has been linked to withdrawal symptom variability, suggesting that smokers with a history of depression are more "reactive" to stressors during withdrawal than smokers without a history of depression (Piasecki, Jorenby, Smith, Fiore, & Baker, 2003). The finding that depression is a robust moderator of nicotine withdrawal has important clinical and research implications, especially given the high comorbidity rates between depression, other Axis I disorders, Axis II issues, and certain medical conditions (e.g. chronic pain).

Anxiety.

Comorbidity rates between anxiety and nicotine dependence are striking given that smokers are 1.6 times more likely to meet criteria for an anxiety disorder than never smokers (Morrell & Cohen, 2006). However, despite these alarming rates, relatively little is known regarding the effects of comorbid anxiety on nicotine withdrawal experience. However, the limited research findings suggest that individuals who have anxiety

symptoms generally report elevated levels of withdrawal related anxiety during cessation. Specifically, individuals with a history of panic attacks report elevated anxiety symptoms during cessation, including concentrating difficulties, irritability, and restlessness compared to individuals who do not report panic attacks (Zvolensky, Lejuez, Kahler, & Brown, 2004b). Additionally, individuals with high trait-anxiety report increased anxiety related withdrawal symptoms including irritability, difficulty concentrating, restlessness, worry, and state anxiety (Becona, Vazquez, & Miguez, 2002; C. S. Pomerleau et al., 2000). Finally, there is some evidence to suggest that anxiety modifies retrospective reports of withdrawal severity, with individuals who are reactive to anxiety (as seen in panic disorder) reporting more severe withdrawal retrospectively than those who are less reactive to anxiety (Zvolensky et al., 2004a). However, given the limited attention the relationship between anxiety and nicotine withdrawal has received, continued research is warranted.

Schizophrenia.

Individuals with schizophrenia are more likely to smoke than any other group with comorbid Axis I or II diagnosis (Lyon, 1999), with between 60% and 90% of individuals with schizophrenia also smoking cigarettes (Tidey, O'Neill, & Higgins, 1999). These figures are even more staggering given that individuals with schizophrenia are also more likely to be heavy smokers, smoke cigarettes with a high nicotine yield, and have considerable difficulty abstaining (Jarvis, 1994; Lyon, 1999). However, comorbid schizophrenia does not appear to moderate the experience of nicotine withdrawal or craving compared to non-psychiatric controls (once smoking level is controlled) (Tidey,

Higgins, Bickel, & Steingard, 1999). This finding suggests that individuals with schizophrenia may smoke for reasons which differ compared to other diagnostic groups.

Alcohol abuse and dependence.

While approximately 80% of alcohol dependant individuals also smoke cigarettes (Gulliver, Kamholz, & Helstrom, 2006), relatively little is known about the relationship between comorbid alcohol use and nicotine withdrawal. The finding is likely due to the fact that alcohol use disorders are generally considered a higher treatment priority, despite the fact that smoking produces higher mortality and morbidity rates (Gulliver et al., 2006). However, despite the dearth of available research, a few important findings have been reported. First, nicotine and alcohol use appear to have a reciprocal relationship, in that use or dependence on one drug significantly predicts use or dependence of the other (Henningfield, Clayton, & Pollin, 1990; Hughes & Kalman, 2006; Hurt, Dale, Offord, & Croghan, 1995; Marks, Hill, Pomerleau, Mudd, & Blow, 1997; McKee, Krishnan-Sarin, Shi, Mase, & O'Malley, 2006). Second, there appears to be no direct moderating effect of alcohol use disorders on nicotine withdrawal severity (Hughes, 1993; Hurt et al., 1995; Marks et al., 1997). Third, alcohol use disorders predict increased nicotine dependence, which in turn predicts increased withdrawal severity (Marks et al., 1997). Finally, visual and olfactory alcohol cues trigger smoking urge (Rohsenow, Monti, Colby, & Gulliver, 1997). These findings support the notion that the relationship between comorbid smoking and alcohol use disorders is clinically important.

Personality disorders.

Individuals diagnosed with personality disorders, including borderline, antisocial, and schizotypal personality disorders are at increased risk for smoking (Serman, Johnson,

Geller, Kanost, & Zacharapoulou, 2002; Tanskanen, Viinamaki, Koivuma-Honkanen, Jaaskelainen, & Lehtonen, 1998; Trull, Waudby, & Sher, 2004). Despite this, research investigating the moderating effects of these disorders on withdrawal symptoms is generally lacking. However, it is reasonable to infer that individuals with these personality disorders likely experience more severe nicotine withdrawal, given that comorbid Axis I disorders including depression and anxiety are common, and some Axis II personality characteristics have been linked to increased withdrawal severity (e.g. impulsivity: VanderVeen, Cohen, Cukrowicz, & Trotter, 2008). Further research in this area is clearly warranted.

Smoking quantity.

Smoking quantity has been linked to nicotine withdrawal experience. Specifically, smoking quantity is negatively related to withdrawal symptom onset latency, as well as elevated sleep disturbance, fatigue, general withdrawal severity, smoking craving, mood disturbance, and depression (Fernando, Wellman, & DiFranza, 2006; Hughes, 1992; Panday, Reddy, Ruiter, Bergstam, & de Vries, 2007; Shiffman et al., 1995). However, these findings only hold true for low levels of cigarette use (i.e. 10 or fewer cigarettes per day). For smokers using more than 10 cigarettes the relationship between smoking quantity and withdrawal severity disappears (Shiffman et al., 2006). This finding has important research implications, as it can provide guidelines to investigators regarding study inclusion criteria.

Gender and Withdrawal

The literature consistently demonstrates that woman are generally less likely than men to successfully abstain from smoking (Perkins, 2001). This difference in gender may

be the result of multiple processes including different smoking withdrawal expectancies (e.g. fear of weight gain), smoking to regulate affect, and lower motivation and confidence to quit (Schnoll, Patterson, & Lerman, 2007). However, it is unclear how gender affects the withdrawal experience. Specifically, the research examining gender differences in withdrawal experience have found mixed results. Some studies have demonstrated that women experience more severe withdrawal compared to men (Hatsukami, Skoog, Allen, & Bliss, 1995; Leventhal et al., 2007). Other reports have failed to find these gender differences (Hughes, 1992; Hughes, Gust, Skoog, & Keenan, 1991; Tate, Pomerleau, & Pomerleau, 1993). It has been suggested that these mixed findings may be the product of differential reporting between genders in terms of retrospective and prospective withdrawal assessment (C. Pomerleau, Tate, Lumley, & Pomerleau, 1994). For example, in a study assessing nicotine withdrawal severity, Pomerleau and colleagues (1994) found no gender differences in prospectively measured withdrawal, but found that women reported higher withdrawal severity than men retrospectively. While subsequent research has generally supported this notion, mixed results continue to be reported (Hogle & Curtin, 2006; Leventhal et al., 2007).

Further complicating the mixed findings on gender and nicotine withdrawal are the hormone and somatic functioning fluctuations associated with the menstrual cycle. Specifically, there is an emerging body of literature on the effects of the menstrual cycle on nicotine withdrawal. While there are some mixed findings in this literature (Allen, Hatsukami, Christianson, & Brown, 2000; Allen, Hatsukami, Christianson, & Nelson, 1999; Perkins et al., 2000; Snively, Ahijevych, Bernhard, & Wewers, 2000), a recent literature review by Carpenter, Upadhyaya, LaRowe, Saladin, and Brady (2006)

tentatively concluded that withdrawal symptom severity is elevated during the late luteal phase (pre-menstrual phase) compared to other menstrual phases. However, caution should be used with their conclusion as there is considerable overlap between nicotine withdrawal symptoms and symptoms commonly reported during the late luteal phase (e.g. irritability, low mood, anxiety) (Carpenter, Upadhyaya, LaRowe, Saladin, & Brady, 2006). Given that this is a relatively new line of research and the mixed findings, continued research is warranted.

Readiness to Change

Motivation is an important factor which predicts when, if, and how smokers make the choice to quit (Van Der Rijt & Westerik, 2004). One of the best researched and most widely accepted models of motivation and change is known as the Transtheoretical Model, and was proposed by Prochaska and Diclemente (1982).The Transtheoretical Model is an integrative motivation model which asserts that behavioral change occurs as a function of *stages* and *processes* (Prochaska & DiClemente, 1982).

Prochaska, DiClemente, and Norcross (1992) defined five *stages* of change which describe when behavior change occurs. These stages include pre-contemplation, contemplation, preparation, action, and maintenance. The pre-contemplation stage describes individuals who have no intent to change in the near future, and who likely have poor insight into the problem behaviors. The contemplation stage of change describes individuals who are aware of problems, but have marked ambivalence toward making a commitment to change. These individuals are likely to “straddle the fence,” teetering back-and-forth without making any significant movement toward change. In the preparation stage individuals have committed to change within the next month, and have

often begun to make small changes toward their goal. In the action stage individuals have changed their target behavior (e.g. smoking cessation) for between 1 day and 6 months. Finally, the maintenance stage is when the target behavior has been maintained for more than 6 months. These stages can be conceptualized as both discrete stages (Prochaska, DiClemente, & Norcross, 1992), and as a continuum (Spencer, Pagell, Hallion, & Adams, 2002).

While the five *stages* of change describe when behavior change is likely to occur, the *processes* of change describe how behavior change occurs (Prochaska & DiClemente, 1982). Through a synthesis of the major therapeutic paradigms, Prochaska and colleagues (1992) identified 10 processes of change which correspond to inter-stage transitions. These processes include consciousness raising, self-reevaluation, self-liberation, counterconditioning, stimulus control, reinforcement management, helping relationships, dramatic relief, environmental reevaluation, and social liberation. In general, research has found that during early stage transitions individuals tend to rely on cognitive (i.e. consciousness raising, environmental reevaluation) and affective (i.e. dramatic relief) processes. However, during late-stage transitions individuals use behaviorally oriented change processes (i.e. reinforcement management, helping relationships, counterconditioning, stimulus control) (Prochaska & DiClemente, 1982; Spencer et al., 2002).

While the Transtheoretical Model remains popular, recent work has highlighted significant conceptual problems with the theory. Specifically, it appears that the boundaries between stages are ill defined, in that it is difficult to find discontinuity between the precontemplation, contemplation, and action stages of change (Balmford,

Borland, & Burney, 2008; Herzog, 2008; Herzog & Blagg, 2007). This lack of discontinuity may result from arbitrary time designations between stages (Herzog, 2008), and stage of change subtypes within precontemplation and contemplation (Anatchkova, Velicer, & Prochaska, 2006; Balmford et al., 2008; Herzog, 2008). Further research is clearly needed to resolve these issues.

Despite the recent criticism, the stages of change have important treatment implications. Specifically, specific *processes* of change theoretically facilitate movement between different *stages* of change. Therefore, interventions which focus on stage-matched processes are likely to be more effective than non-staged match interventions. This notion is generally supported in the literature, with the majority of published studies finding stage matched interventions more effective than stage miss-matched interventions, or treatment as usual (Spencer et al., 2002). However, contrary findings have also been noted, with other researchers demonstrating that stage-match interventions provide little advantage over stage-mismatched interventions (Bridle et al., 2005; Sutton, 2001). These inconsistent findings are unsurprising give that a surprisingly large proportion of published studies in this area have used questionable or poor methodologies (Bridle et al., 2005; Spencer et al., 2002; Sutton, 2001). Therefore, there is a clear need for additional high quality research in this area.

Section 2: A Brief Overview of Chronic Pain

As stated above, chronic pain constitutes a serious public health problem. Therefore, research focusing on factors that influence pain experience is important. The discussions that follow provide brief reviews of the epidemiology of pain, pain theories,

the two major pain categories, and physiological and psychological factors which effect pain. These reviews are included to provide a context for the above proposed study.

Epidemiology of Pain

Chronic pain is a serious public health concern, as it affects approximately 10 to 20% of the general population (Gatchel et al., 2007). Furthermore, pain affects over 50 million Americans, costs the American public $70 billion dollars annually, and accounts for approximately 80% of all physician visits (Gatchel et al., 2007). Finally, chronic pain places a significant burden on work productivity, as it accounts for approximately 15% of lost work days and 18% of early retirements (Pfingsten & Hidebrandt, 2004: as cited by Schneider, Schiltenwolf, Zoller, & Schmitt, 2005; Tüzün, 2007).

While the societal costs of chronic pain are troublesome, the individual costs are staggering. Specifically, chronic musculoskeletal pain is associated with lower quality of life across multiple domains including physical health, mental health, and social functioning (Tüzün, 2007). Physical health problems commonly co-occurring with chronic pain include decreased physical functioning, decreased muscle strength/flexibility, increased sleep disturbance, and increased fatigue (Tüzün, 2007). Chronic pain is also associated with serious medical problems including HIV disease, diabetes, and hepatitis C (Gran, 2003). Psychological costs of chronic pain include increased associations with depression, fear, anxiety, anger, and personality disorders (Gatchel et al., 2007; Tüzün, 2007). Finally, chronic pain has been linked to decreased social functioning (e.g. decreased time spent with family and friends, costs associated with medical interventions) (Tüzün, 2007).

Pain Theory

The two primary medical epistemologies in the United States include the biomedical and biopsychosocial models (Evans & Trotter, 2009). The biomedical model is the most common, and operates under the assumptions of mind-body dualism and biological reductionism. Specifically, this model assumes that there is no interaction between psychological processes and physical functioning, and that disorder or dysfunction can be ultimately understood by breaking an organism into its most basic parts. While this model has been influential, it is often limited in its ability to explain complex medical problems, especially when psychological or behavioral characteristics play an important role in pathology (Evans & Trotter, 2009). The biopsychosocial model, originally proposed by Engel (1980), operates under the assumptions made by a general systems theory. Specifically, it assumes that there is a complex relationship between the mind and body, and that medical problems are a biological, psychological, and social experience (Evans & Trotter, 2009). Given the inadequacy of the biomedical model in explaining chronic pain, the last three decades have seen a considerable shift towards the biopsychosocial theories of pain experience (Gatchel et al., 2007).

One early pain theory which moved away from a strict biomedical perspective was the Gate Control Theory of Pain (GCTP; Melzack & Wall, 1965). In the development of this theory, Melzack and Wall (1965) recognized that a comprehensive pain model must not only include a biological mechanism for pain experience, but must also allow for the moderating effects of emotion and cognitive evaluation (Gatchel et al., 2007). The GCTP postulates that the transmission and processing of pain signals to the

spinal cord occur as the result of a 5 stage process. These stages include: 1) the pain signal is sent, via the peripheral nervous system, to the spinal cord, 2) this signal then activates an interneuron in the spinal cord region, 3) additional pain peripheral nervous system signals are received for potential processing in the spinal cord, 4) inhibitory interneurons are activated within the spinal cord, and finally, 5) a loop system is established in which ascending pain signals sent to the brain are influenced by descending signals sent from the brain (Gatchel et al., 2007). This theory paved the way for additional comprehensive pain models.

A more contemporarily biopsychosocial pain theory is the Neuromatrix Theory of Pain (NTP; Melzack, 2001). The NTP states that pain experience is the result of a large neuro-network in the brain called the "body-self neuromatrix." This theory proposes that pain experience is a function of integrated processing between cognitive-evaluative, sensory-discriminative, and motivational-affective systems within this large neuromatrix (Gatchel et al., 2007). Furthermore, this theory stresses that the pain response (i.e. via perceptual, behavior, and homeostatic systems) is the result of this large integrated neuro-network, and not simply a direct response to a sensory input (Gatchel et al., 2007). This theory is important, as it integrates not only biological processes, but also affective and cognitive processes in the experience of pain.

Types of Pain

Chronic pain experience, which is loosely be defined as pain lasting more than 3 months (Robinson, 2007), can be divided into the two broad categories; musculoskeletal and neuropathic pain. These two types of pain result from different tissue damage and constitute different physiological sensations. The review that follows describes these pain

categories separately. However, it is important to note that the experience of these pain types is not mutually exclusive, as it is possible for someone to experience both.

Musculoskeletal pain.

Musculoskeletal pain is the result of musculoskeletal dysfunction. While musculoskeletal disorders are broad in nature, they can be categorized into common groups including osteoporosis (and associated features), spinal disorders (e.g. low back pain), arthritic disorders (e.g. osteoarthritis and rheumatoid arthritis), and other musculoskeletal injuries (e.g. high-energy limb fractures, strains, and sprains) (Kelsey & Hochberg, 1988; Walsh et al., 2008). Each of these disorders is characterized by some form of mechanical damage (i.e. either muscle or bone damage). Osteoporosis is an overall weakening of bone structures which increases susceptibility to fractures. Fractures are common in the hip, vertebrae, distal radius, humerus, and pelvis. Risk for osteoporosis increases with age, and is more likely in women than men (Kelsey & Hochberg, 1988). Spinal disorders (including low back pain) are very common, and are caused by a variety of problems including strains, sprains, disc herniations, and facet abnormalities (Kelsey & Hochberg, 1988; Walsh et al., 2008). While approximately 60 to 80% of the population is affected by back pain at some point in their life, 90% of conditions resolve within a month, and only 7% continue after 6 months. Back pain is commonly caused by life style factors (e.g. work habits, lifting and twisting) (Kelsey & Hochberg, 1988). Arthritic disorders are characterized by inflammation in the joints which includes stiffness, pain, and occasional swelling. There are over 100 diseases that can cause arthritic disorders (Kelsey & Hochberg, 1988). Finally, other musculoskeletal disorders are common, and may include shoulder, knee, and hip problems (Walsh et al.,

2008). Musculoskeletal pain is often described as sharp, dull, or aching (e.g. see McGill Pain Questionnaire; Dworkin et al., 2009).

Researchers have identified several factors associated with increased risk for chronic musculoskeletal pain, many of which are specific to disorders. However, certain demographic and behavioral risk factors appear to transcend many of these disorders. For example, women are more likely to report chronic pain, and seek treatment, than men. This finding is consistent with low back pain, chronic widespread musculoskeletal pain (like that seen in fibromyalgia), shoulder pain, and osteoporosis (and associated bone fractures) (Gran, 2003; Kelsey & Hochberg, 1988; McBeth & Jones, 2007). Additional demographic variables which influence chronic musculoskeletal pain risk include increased age, lower socioeconomic status, and ethnic minority status (African Amerian and Hispanic) (Gran, 2003; McBeth & Jones, 2007). Behavioral factors which transcend many of these conditions include cigarette smoking and obesity (McBeth & Jones, 2007).

Neuropathic pain.

Neuropathic pain is defined as "[pain] initiated or caused by a primary lesion or dysfunction in the nervous system" (Merskey & Bogduk, 1994). In other words, neuropathic pain is the result of damage or dysfunction in either peripheral or central nerves. Nerve damage, leading to neuropathic pain, can be caused by a number of processes. For example, peripheral nerve damage can be caused by diabetes, HIV, chemotherapy, viral infection, amputation (i.e. phantom limb pain), and surgery (Dworkin, 2002). Central neuropathic nerve damage can be caused by stroke, multiple sclerosis, Parkinson's disease, or spinal cord injury (Dworkin, 2002). Neuropathic pain is

frequently described as electric shock, burning, cold, pricking, tingling, and itching pain (Dworkin, 2002).

Neuropathic pain can be broken into two broad categories including spontaneous pain, and stimulus-evoked pain. Spontaneous pain occurs without stimulation, and can be either intermittent or continuous. Stimulus-evoked pain occurs following an applied stimulus. There are a number of stimulus-evoked pain categories including allodynia (pain resulting from stimuli which do not typically evoke pain, e.g. light touch), analgesia (absence of pain response when pain should occur), and hyperalgesia (exaggerated pain response to painful stimuli) (Dworkin, 2002).

Physiological Pain Factors: Musculoskeletal Pain

One neurological mechanism believed to play an important role in chronic pain is central and peripheral nervous system sensitization. Specifically, research over the past 20 years has demonstrated that nociceptive input (resulting from noxious stimuli) can lead to expansion of receptive fields in the brain, a reduction of neuron firing threshold, and spontaneous neuronal firing even after the stimuli is removed (Robinson, 2007). While the majority of this research has been done with animals (due to obvious ethical reasons), this process is believed to be mirrored in humans (Robinson, 2007). Furthermore, researchers have hypothesized links between central nervous system sensitization to a number of specific chronic pain disorders in humans including chronic headache, fibromyalgia, and chronic spinal pain (Robinson, 2007).

Given the advances in the past 40 years in neuro-imaging techniques, researchers have identified a number of brain regions which have been implicated in acute and chronic pain perception. For example, using positron emission tomography (PET) scans

researchers have identified that acute thermal pain leads to activation in the primary and secondary somatosensory cortex, anterior insula, anterior cingulated cortex, prefrontal cortex, supplemental motor cortex, basal ganglia, cerebellum, and the hypothalamus (Gatchel et al., 2007). Additionally, functional magnetic resonance imaging (fMRI) studies have identified blood flow changes in several brain regions during chronic pain experience including the thalamus, caudate, frontoparietal region, anterior cingulated cortex, and the contralateral somatosensory cortex. The broad range activation seen with pain induction includes areas known to be important in affective and cognitive processing, suggesting that these processes are important to the pain experience (Gatchel et al., 2007).

Psychological Pain Factors: Musculoskeletal Pain

Psychological factors are now widely accepted as major contributors of the chronic pain experience (Robinson, 2007). For example, The International Association for the Study of Pain has stated that pain "is unquestionably a sensation in a part or parts of the body but is also always unpleasant and therefore also an emotional experience" (page 1; Merskey, 1986). The acceptance that psychological factors influence pain experience is also evidenced by the fact that several recent literature reviews of chronic pain include discussions of psychological moderators (e.g. Gatchel et al., 2007; Gran, 2003; McBeth & Jones, 2007; Sen & Christie, 2006). This widespread acceptance has lead to the inclusion of many behavioral scientists (i.e. psychologists and social workers) in multidisciplinary pain management clinics (Robinson, 2007).

Chronic pain is affected by a wide array of psychological dysfunction. For example, several diagnosable disorders including anxiety disorders, depression,

personality disorders, and substance use problems have been shown to moderate chronic pain experience (Robinson, 2007). Additionally, dysfunctional affective responses (which do not meet criteria for an Axis I or II disorder) play a significant role in the pain experience (Gatchel et al., 2007; Robinson, 2007).

Considerable research has focused on the effects of depression, anxiety (including fear), and anger on the experience of chronic pain. Specifically, depression has been shown to share a negative reciprocal relationship with chronic pain, in that experience of either problem can cause/exacerbate the experience of the other (Rudy, Kerns, & Turk, 1988). Depression has also been associated with increased pain severity in chronic pain patients (Dworkin et al., 1992). Anxiety is a common emotion in chronic pain patients. Pain patients may feel anxiety and fear for a number of reasons including (for example) anxiety about the meaning of their pain, fear that their symptoms will lead to permanent disability, fear that certain activities will increase pain, and a general fear of the pain experience (Gatchel et al., 2007). Fear and anxiety can have serious negative consequences for chronic pain. For example, fear and anxiety can cause avoidance of certain activities associated with increased pain. In turn, avoidance is negatively reinforced via pain and fear reduction. Therefore, avoidance may ultimately lead to a limiting of activity levels, thus increasing disability and ultimately exacerbating pain experience (Gatchel et al., 2007). Finally, anger is a common emotion in individuals with chronic pain. For example, in a sample of pain patients referred to a multidisciplinary pain rehabilitation center, 98% reported some level of anger (Okifuji, Turk, & Curran, 1999). Participants in this study reported that their anger was focused towards health care providers, significant others, insurance companies, employers, attorneys, and towards

themselves. These feelings of anger are important, as they have been linked to pain severity and frequency of pain behaviors (Kerns, Rosenberg, & Jacob, 1994; Summers, Rapoff, Varghese, Porter, & Palmer, 1991). While this summary only scratches the surface of the effects of affective dysfunction on chronic pain experience, one thing is for certain, is it is not possible to fully understand and manage chronic pain if you do not understand and treat the affective counterparts.

Section 3: Chronic Pain and Smoking

Smoking and Chronic Pain

Smoking is often comorbid with other health and wellness issues. For example, smoking is over represented in the population of individuals diagnosed with mood and psychotic disorders (Morrell & Cohen, 2006; C. S. Pomerleau et al., 2000), with smokers being two times more likely to report a history of depression compared to their non-smoking peers (Covey et al., 1990; J. R. Hughes, Hatsukami, Mitchell, & Dahlgren, 1986; Morrell & Cohen, 2006), and individuals with schizophrenia being three times more likely to smoke than individuals with other comorbid psychological disorders (Kisely, Preston, & Shannon, 2000). The same is true for chronic pain and smoking. Specifically, individuals who suffer from chronic pain are more likely to smoke then their pain free counterparts. For example, approximately 28.6% of the U.S. population over the age of 12 reports using tobacco within the past month (NIDA, 2009); however, and an estimated 54% of individuals with chronic low back pain are classified as smokers (Jamison, Stetson, & Parris, 1991).

The finding that smoking and chronic pain are often comorbid is particularly troublesome as each condition is independently associated with numerous health and

functioning concerns. For example, smoking in isolation negatively affects quality of life, decreases surgical success, is related to increased negative effect, and causes numerous health problems (US DHEW, 1964; Vogt, Hanscom, Lauerman, & Kang, 2002). Further, chronic pain in isolation is related to decreased quality of life, decreased functioning, as well as other negative health indicators (Gran, 2003; Robinson, 2007; Tüzün, 2007). However, the health effects of smoking and chronic pain combined are particularly troublesome. For example, in addition to the other well documented health effects, smoking has been associated with accelerated bone loss, spinal disk degeneration, and restricted blood flow vertebral tissues, which can exacerbate pain experience (Vogt et al., 2002). Additionally, smokers with chronic pain reportedly use more pain medications and are less likely to experience pain improvement following spinal surgery compared to their non-smoking peers (Barton, Kofoed, & Doleys, 1989; Jamison et al., 1991; Vogt et al., 2002). Finally, smoking and chronic pain are both associated with psychological dysfunction (e.g. depression, anxiety: Fishbain et al., 2007; Kamaleri, Natvig, Ihlebaek, Benth, & Bruusgaard, 2008; Morrell & Cohen, 2006). These findings suggest that smokers with chronic pain are at an increased risk for morbidity and mortality; therefore, this population should be considered a high priority in terms of smoking cessation treatment research.

Nicotine Analgesia

Despite the fact that comorbid smoking and chronic pain produce significant health and functioning deficits, the literature investigating the link between chronic pain and smoking is relatively modest. However, recent evidence suggests that laboratory induced pain increases craving to smoke and reduces latency to smoke following painful

versus non-painful cold pressor procedures (Ditre & Brandon, 2008). This finding highlights the relationship between smoking and pain experience, and suggests that smoking may moderate the experience of pain or provide a means of coping. The notion that nicotine moderates pain experience has been repeatedly demonstrated in the literature. The existing literature on the moderating effects of nicotine on pain suggests a number of important findings, which are outlined below.

Nicotine analgesia: general support.

Researchers have demonstrated that nicotine administration generally decreases pain experience, which has been observed in both laboratory and community-based research. For example, in a well controlled series of laboratory studies, Perkins and colleagues (1994) investigated the effect of nicotine administration (via nicotine nasal spray) on thermal pain detection across three studies. These three studies differed by the sample utilized (i.e. smokers and non-smokers), by nicotine dose administered, and by pain detection timeframe. Across all three studies, the authors found that nicotine administration consistently increased latency to detect thermal pain (in seconds) (Perkins et al., 1994). These findings suggest that nicotine moderates pain experience. Other laboratory-based studies have found similar results. Specifically, researchers have demonstrated that nicotine administration (smoking, snuff, or nicotine nasal spray) increases pain threshold (i.e. the point at which pain is first detectable) and pain tolerance (i.e. the maximum level of pain one can willingly withstand) (Girdler et al., 2005; Jamner, Girdler, Shapiro, & Jarvik, 1998; Lane, Lefebvre, Rose, & Keefe, 1995). Additionally, these findings are consistent across a variety of pain induction techniques including thermal pain (heat), cold pressor pain (submersion of arm in to ice water), and

tourniquet ischemia pain (halting limb blood circulation using a blood pressure cuff). Research using electric shock pain has also shown nicotine analgesia; however, results from this literature are mixed (Jamner et al., 1998; Knott, 1990; Sult & Moss, 1986), suggesting that nicotine may not moderate the experience of all types of pain.

Studies using community-based paradigms have also supported the link between pain and nicotine. For example, John and colleagues surveyed a population-based sample of 4075 German adults. This survey assessed smoking behavior, nicotine dependence, and pain experience (severity and location). They found that that heavy smokers tend to report less severe pain than lighter smokers (John, Meyer, Rumpf, & Hapke, 2009), suggesting that nicotine produces an analgesic effect at higher concentrations.

Nicotine analgesia: pain reduction versus withdrawal symptom reduction.

The analgesic effects of nicotine administration appear independent of withdrawal reduction (Fertig, Pomerleau, & Sanders, 1986). Specifically, Fertig and colleagues (1986) assessed the effects of nicotine administration (via nicotine cigarette and snuff) on pain detection in a mixed design. In their two part examination, male smokers and ex-smokers were recruited. In the first study, smokers were asked to participate in 2 nicotine administration conditions (smoking and nicotine snuff) and 2 control conditions (sham smoking and smoking a non-nicotine cigarette). In the second study, ex-smokers participated in 1 nicotine administration condition (nicotine snuff) and 1 control condition (nicotine free powder). In both studies pain was induced via cold pressor. Pain experience was assessed with the McGill Pain Questionnaire, and via pain detection (latency to detect pain) and tolerance (latency to arm removed from cold water) measurements. Nicotine withdrawal was assessed via two nicotine withdrawal

questionnaires. Results from study 1 indicated that nicotine administration (smoking and snuff) decreased pain experience (e.g. detection, tolerance, and McGill Pain Questionnaire scores), but did not affect nicotine withdrawal severity. Similar results were seen in study 2, where nicotine administration reduced self-reported pain severity as well as pain tolerance (no effect was seen for pain detection). These results suggest that the analgesic effects of nicotine are independent of its withdrawal reduction effects. The independence of nicotine analgesia and withdrawal reduction has also been reported in other studies (e.g. Perkins et al., 1994).

Nicotine analgesia: the pain-type dependence of nicotine analgesia.

Nicotine's analgesic effects are not constant across all types of pain. Specifically, while nicotine moderates the experience of musculoskeletal pain (i.e. structural damage), it does not appear to moderate the experience of neuropathic pain (i.e. pain caused by damaged or dying nerves) (Benbow, Williams, & MacFarlane, 1997). Specifically, Bendow and colleagues (1997) found no evidence for an analgesic effect of nicotine in individuals who suffered from pain resulting from diabetic neuropathy. This finding suggests that smokers with predominantly neuropathic pain likely smoke for reasons other than pain reduction. Additionally, it should be noted that neuropathic pain can be described as "electric shock pain" (e.g. see McGill Pain Questionnaire; Dworkin et al., 2009). Therefore, there is likely a relationship between the findings described by Bendow and colleagues (1997), and the inconsistent findings regarding the analgesic properties of nicotine to reduce electric shock pain.

Nicotine analgesia: analgesic dose-response.

There appears to be a complex dose-response relationship between nicotine consumption and analgesia. Specifically, findings from laboratory and community-based research evidence a relationship between cigarette consumption (measured via multiple markers) and experience of pain. In a laboratory-based study, Knott (1990) investigated the relationship between smoking and subjective (self-report) and objective (brain evoked potentials) markers of pain, in a group of female smokers. During his initial analysis (repeated measures ANOVA), he found no relationship between smoking and non-smoking conditions in terms of subjective pain experience (analysis with objective markers of pain were significant in the expected direction). However, he did find a negative correlation between cigarette consumption (measured via expired CO) and subjective markers of pain, suggesting that higher dose of nicotine lead to greater pain reception. In a later study, Perkins and colleagues (1994) investigated the effects of nicotine dose (i.e. 0, 5, 10, or 20 ug/kg every 30 minutes for 2 hours) on pain perception between smokers and non-smokers (Perkins et al., 1994). Using regression analysis, these researchers found a significant positive relationship between pain latency and plasma nicotine levels (Study 3). Taken together, these results suggest that the analgesic properties of nicotine are dose dependent.

Descriptive community-bases studies paint a slightly different picture, as many researchers have reported positive relationships between smoking consumption (measured via number of pack years and years smoking), nicotine dependence level, and pain severity (Andersson, Ejlertsson, & Leden, 1998; Goldberg, Scott, & Mayo, 2000; Scott, Goldberg, Mayo, Stock, & Poîtras, 1999; Weingarten et al., 2008; Zimmermann-

Stenzel, Mannuay, Schneider, & Schiltenwolf, 2008). In addition to these findings, John and colleagues (2009) surveyed a large sample of German smokers found that current heavy smokers (using 20 or more cigarettes per day) generally reported less pain than former smokers. Taken together, these findings suggest two things: first, as pain increases smoking level also increases, and second, heavy smoking leads to decreased pain risk. While these results appear somewhat contradictory to the laboratory-based studies described earlier, one possible interpretation is that as pain severity increases use of nicotine for analgesic purposes also escalates to compensate.

Nicotine analgesia: effects of gender.

It has been suggested that the analgesic properties of nicotine effect men and women differentially. The initial evidence for this finding came from several early studies investigating pain and smoking. Specifically, several studies using male samples found that nicotine administration consistently decreased pain perception (e.g. Fertig et al., 1986; Pauli, Rau, Zhuang, & Brody, 1993), while others studies failed to find such results with female samples (e.g. Sult & Moss, 1986). However, despite these inconsistent gender findings, few early studies on nicotine and pain perception either included gender comparisons in their analysis, or enrolled sufficient numbers or both sexes to perform meaningful gender comparisons. To address these short comings, Jamner at colleagues (1998) investigated the relationships amongst pain perception, nicotine administration, and gender. In their study, they utilized a large sample of male and female smokers and non-smokers, and electrical stimulation to induce pain. Consistent with the early literature, their results indicated that nicotine (administered via nicotine patch) increased pain threshold in men but had no effect in women. The authors

concluded that while the direct mechanisms through which gender differentially predicts nicotine's analgesic effects is unknown, these differences may be the result of physiological differences (e.g. menstrual cycle, blood pressure differences).

These findings and conclusions were later re-tested and expanded by Girdler and colleagues (2005) who also investigated the relationships amongst pain, gender, and nicotine. These researchers investigated this relationship using a large sample of male and female smokers, and by utilizing a variety of pain induction techniques (e.g. thermal, cold pressor, and tourniquet ischemia). Nicotine was administered via paced smoking. Their results suggested that the relationship between nicotine analgesia and gender was dependent on the type of pain induced, with women demonstrating a nicotine analgesic effect with ischemic pain, and men demonstrating the effect with cold pressor pain (no differences found for thermal pain). They concluded that these gender dependent effects were likely the result of neuroendocrine mechanisms (e.g. decreased estrogen concentrations in female smokers and increased plasma norepinephrine in male smokers). Further, they concluded that the previous inconsistencies in the literature regarding nicotine analgesia, pain, and gender were likely the result of varied study methodologies (e.g. including pain induction, nicotine administration, and population) and a failure to include enough women in studies to conduct gender analysis.

While the results of Girdler and colleagues (2005) are compelling, their conclusions should be considered with caution. Specifically, they did not include electrical stimulation pain induction in their study. This is problematic, as a large portion of smoking and pain studies have used electrical stimulation for pain indication (e.g. Jamner et al., 1998). Additionally, their finding that nicotine administration had no effect

on thermal pain experience was inconsistent with previous findings (Lane et al., 1995). Therefore, while it is clear from the Girdler and colleagues (2005) study that nicotine does effect pain perception in women; considerable research is still needed to fully describe gender differences. However, based on the literature as a whole, a few tentative conclusions can be made. Specifically, nicotine may act as a more consistent analgesic in men than in women, as the bulk of the literature continues to support the notion that the analgesic effects of nicotine are more pronounced in men than women (Jamner et al. 1998). Additionally, the analgesic process of nicotine may affect a broader range of pain in men (i.e. cold pressor, electrical stimulation, thermal pain) than woman (ischemic pain) (Girdler et al., 2005; Jamner et al., 1998; Perkins et al., 1994).

Readiness to Change and Chronic Pain

As stated above, a clear understanding of the factors which influence an individual's readiness to change with regard to quitting smoking would aid in smoking cessation treatment. As nicotine consumption moderates pain experience, it is likely that smoking behavior is negatively reinforced among individuals who suffer from chronic pain (Girdler et al., 2005; Jamner et al., 1998; Lane et al., 1995). Therefore, it is reasonable to assume that pain experience affects smokers' readiness to quit smoking. As outlined above, Prochaska, DiClemente, and Norcross (1992) have defined 5 stages which outline the process of behavior change (i.e. pre-contemplation, contemplation, preparation, action, and maintenance), and which have direct treatment implications (Spencer et al., 2002). While the relationship between chronic pain experience and stages of change has received little empirical attention, two groups of researchers have investigated this relationship.

In a large cross-sectional survey study, Hahn, Rayes, Kirsh, and Passik (2006) investigated the relationship between pain experience and stage of change. Their sample included 307 adults ranging in age from 18-81 who reported using tobacco products (i.e. cigarettes, pipes, cigars) within the past 30 days. Approximately 29% of their sample smoked more than a pack, 58% smoked one pack or less, and 13% smoked no cigarettes per day. Participants were included in the pain sample if they reported significant pain in the past week (28%; i.e. pain more severe than typical headaches and toothaches), and pain experience was assessed via the Brief Pain Inventory (BPI). BPI scores were compared to stage of change. Results revealed that the majority of participants (58%) were in the contemplation stage or higher, and that there was no relationship between their experience of pain and stage of change. However, numerous methodological flaws were present in this study. First, approximately 70% of the sample smoked one pack of cigarettes or less per day, and 13% smoked zero cigarettes per day, therefore the sample likely included a large proportion of non-dependant smokers. Additionally, the research group defined pain experience as "pain beyond the usual minor headaches, sprains, or toothaches" (p. 476) during the past week. This problematic definition of pain includes individuals who experience acute and/or chronic pain. Therefore, because the negative reinforcing analgesic effects of nicotine likely take time to learn, their inclusion of individuals with acute pain may have increased error variance in the analysis, making it difficult to see a relationship.

Burkhalter, Springer, Chhabra, Ostroff, and Rapkin (2005) also investigated the relationship between readiness to change and pain. Their study included a sample of 428 HIV-infected persons (66% current smokers, 59% male). Using multivariate analysis to

investigate the relationship between several outcome variables and readiness to change, they found that the experience of bodily pain (measured via a single item) was unrelated to readiness to quit smoking. However, similar to Hahn and colleagues (2006), their comparison of pain experience and readiness to quit smoking was suboptimal. Specifically, these researchers did not consider the possible relationship between the chronic nature of pain and readiness to change. Additionally, as noted in their introduction, individuals with HIV disease typically have a "high prevalence of smoking" and a "low readiness to quit" (p. 512) possibly limiting sample variability, and thus the ability to find a relationship between readiness to quit and other variables. Finally, these researchers relied on a single item measure to assess "bodily pain". This single item may not have had the sensitivity or specificity necessary to identify this relationship. In sum, the relationship between chronic pain experience and readiness to quit smoking remains largely unresolved. Elucidation of this relationship is important, as it may have treatment implications for both chronic pain and smoking cessation.

Chronic Pain and Withdrawal

Relatively little is known regarding the relationship between chronic pain and the experience of nicotine withdrawal. This is an important area of study, as the experience of either problem leads to increased risk of the other problem (Jamison et al., 1991; NIDA, 2009), and the issues combined lead to increased morbidity and mortality (Vogt et al., 2002).

Despite the fact that little is known regarding the relationship between nicotine withdrawal and chronic pain, results from two studies suggest that these constructs may be related. Specifically, Andersson, Ejlertsson and Leden (1998) investigated the link

between musculoskeletal pain and smoking in a large sample of Swedish smokers. In this cross-sectional study, the authors compared pain experience to smoking status. Their results showed that widespread pain was associated with feeling depressed, relaxation difficulties, sleep disturbances, and general fatigue. While these symptoms appeared independent of smoking status, their co-occurrence with chronic pain is important, as these symptoms are also included in the DSM-IV-TR Nicotine Withdrawal Syndrome (APA, 2000). Therefore, it is possible that individuals with chronic pain could have increased sensitivity to these symptoms, and are thus prone to experience them during nicotine abstinence.

Additional evidence supporting a link between chronic pain and nicotine withdrawal comes from a study conducted by John, Meyer, Rumpf, and Hapke (2009). In this study, the authors investigated the association between pain experience and the DSM-IV-TR (APA, 2000) nicotine dependence criteria. This cross-sectional survey study included a sample of 4,075 adults from northern Germany. Participants were assessed during a face-to-face meeting with study personnel, and data were collected via computer assisted structured interview. Nicotine dependence was assessed using the DSM-IV-TR criteria, and pain was categorized using ordinal pain categories which combined pain breath (locations) and chronicity. Data were analyzed via a combination of non-parametric (i.e. chi-square) and regression analysis. After adjusting for a number of demographic (age, sex), affective (anxiety and depression), and behavioral (alcohol use) factors, results revealed a positive relationship between pain severity and number of endorsed DSM-IV-TR nicotine withdrawal symptoms. As a result, the authors concluded that nicotine dependence (assessed via withdrawal criteria) was related to increased pain.

While findings from the Andersson and colleagues (1998) and John and colleagues (2009) studies suggest that nicotine withdrawal severity and pain experience may be related, neither study provides a direct comparison between these two constructs. Specifically, Andersson and colleagues (1998) did not include a measure of nicotine withdrawal, as the aim of the study was to elucidate the effects of smoking on chronic pain. Therefore, the only inference (regarding the pain and nicotine withdrawal relationship) that can be made from this study is that smokers with chronic pain may be at increased risk for some nicotine withdrawal symptoms. Finally, John and colleagues (2009) assessed the relationship between nicotine dependence (assessed via DSM nicotine withdrawal criteria) and pain severity. Because their measure of nicotine withdrawal was strongly linked to nicotine dependence, it provides a better measure of withdrawal symptom breadth than severity. Therefore, while evidence exists linking the experience of pain and nicotine withdrawal, the relationship between these two constructs remains largely untested.

Conclusions

Smoking and chronic pain, when considered independently, constitute serious health concerns (Gran, 2003; US DHEW, 1964). Combined however, they put individuals at risk for increased morbidity and mortality (Barton et al., 1989; Vogt et al., 2002). Previous research linking pain experience and smoking/nicotine consumption has primarily been descriptive in nature. This research has been important, and the elucidation of this relationship warrants continued focus. However, as research moves forward, special attention should be paid to processes known to effect the treatment of these problems when they are comorbid. The above literature highlighted several

important factors known to influence the success of smoking cessation treatments (i.e. nicotine withdrawal, gender, and readiness to change), and it linked those factors to co-morbid/co-occurring pain experience. Specifically, this review suggested that chronic pain likely effects withdrawal experience and readiness to change. Additionally, it suggested that gender may moderate the relationship withdrawal experience and stage of change in this comorbid group. The proposed study will test these hypotheses with the hope of informing the treatment of this at-risk population.

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Appendix B: Study Recruitment Challenges

Data collection for this study was met with a number of significant challenges, some of which were amenable to intervention while others we were not. This appendix contains discussions on a number of topics relevant to data collection for this study, including: 1) a review of the steps taken prior to the proposal aimed at increasing recruitment feasibility, 2) a description of the unanticipated barriers faced during recruitment, 3) a discussion of the steps taken during data collection to improve study recruitment and their subsequent recruitment effects, and 4) a brief discussion of study attrition. This appendix is intended to augment the information found in the limitations portion of the main document.

Pre-proposal Efforts to Insure Successful Study Recruitment

Prior to the initiation of data collection, a number of steps were taken in an attempt to insure and/or increase recruitment feasibility. The enumerated list below contains descriptions of those efforts:

1. The investigator was employed in the TTUHSC Family Medicine Department for 4 years prior to recruitment initiation. Additionally, the investigator was a part of the Family Medicine integrated patient care team, as he provided psychotherapy services to medical patients. As a result, the investigator was familiar with the structure of the clinic in ways that facilitated data collection.
2. The investigator gained formal support from key faculty administrators in the Family Medicine Department, including the director of behavioral sciences, the medical residency director, department chair, and associate department chair. These individuals support was invaluable during recruitment and facilitated the integration of research activities into the clinic setting.

3. The investigator gained the support of key clinic staff, including the nurses and clinic administrators. Their support was invaluable and facilitated the integration of research activates into the clinic setting.
4. The investigator was a member of the TTUHSC Family Medicine Pain Clinic. Prior to initiation of recruitment, the investigator informally observed that approximately 50% of the chronic pain patients attending integrated pain clinic visits smoked. Therefore, assuming a 50% study refusal rate and a further 50% attrition rate, we estimated that approximately 1 to 2 participants would be recruited from this clinic each month.
5. The investigator conducted informal interviews with resident and attending physicians to determine the approximate proportion of heavy smokers in the clinic. These physicians estimated that approximately 10% of patients smoked at least 1 pack a day. Given the average daily patient load in the clinic, it was estimated that 11 heavy smokers seen in clinic per day.
6. The investigator was granted study management and recruitment assistance through the TTUSHC Clinical Research Center (CRC). The CRC agreed to assist with chart reviews to identify potential participants.
7. Prior to beginning recruitment, the investigator enlisted the assistance of two graduate students who agreed to assist in data collection. These students were invaluable in the recruitment efforts.
8. Funding for this project was provided through a seed grant from the Laura W. Bush Institute for Women's Health. This award allowed for the reimbursement participants for time and effort.

Unanticipated Barriers to Recruitment (prior to study amendment)

Unanticipated barriers to study recruitment are enumerated below.

1. The estimated proportion of heavy smokers in the clinic was inaccurate. During recruitment in the Family Medicine clinic, we typically identified 1 to 2 heavy smokers per day, not 11 as anticipated. The vast majority of smokers in the clinic reported smoking less that ¾ of a pack to their nurse or physician. It is unclear if the overestimation of smokers in the clinic was due to a saliency bias, or if patients under reported smoking levels to health care providers.
2. No participants were successfully recruited from the Family Medicine Pain Clinic. The reason for this is unclear; however, this clinic saw a shift in physician leadership (the physician co-director left the institution during summer 2010), and we witnessed a relatively high no-show rate (approximately 25%).
3. Many potential participants declined to hear about the study. While there is no formal data on the reasons for participant refusal, anecdotally, patients appeared to decline for work (e.g. they work full time) and health reasons (e.g. they are too sick).
4. The anticipated attrition rate of 50% was inaccurate. This study saw an attrition rate of approximately 67%. The majority of attrition was driven by no-shows. Other reasons include transportation problems, health problems, and participant death (2 participants).
5. Approximately 45% of individuals, who agreed to participate in the study and were consented, did not ultimately meet study criteria and were dropped from participation. This was higher than anticipated.

6. During the course of recruitment, the Family Medicine clinic saw a major change to the scheduling policy. Specially, prior to November of 2010, the Family Medicine Clinic scheduled appointments approximately 3 months in advance. Given that the schedule was relatively stable, study personnel were able to review charts the day prior to scheduled appointments to identify potential participants. This allowed study personnel to come to the clinic at specific times to see specific patients. However, in November 2010 the clinic moved to "open access scheduling." This change meant that that over 80% of the daily appointments were scheduled the day before or the day of the appointment. Given that the schedule changed minute to minute, study personnel were required staff the clinic all day to identify and recruit participants. This change significantly increased recruitment burden, and decreased efficiency.

Recruitment numbers resulting from the Family and Community medicine clinic are outlined in Appendix B, Table 1.

Efforts to improve recruitment

Listed below are strategies employed to improve study recruitment:

1. Additional study personnel were secured to increase recruitment efforts. This increased the number of hours we could recruit in the Family Medicine Clinic and the International Pain Center.
2. In October of 2010, recruitment began at the Impact Lubbock Free Clinic (staffed primarily by Family Medicine physicians). This clinic met once a week in the evenings.

3. Meetings with Dr. Cohen occurred frequently during late summer and fall of 2010 to discuss recruitment efforts.
4. The International Pain Center was opened as a recruitment site in April, 2011. Recruitment procedures in this clinic mirrored those in the Family Medicine Clinic.
5. Recruitment flyers were posted at TTU and TTUHSC beginning in March, 2011. Participants responding to these ads were screened over the telephone.
6. Recruitment ads were placed in local news papers March through May of 2011. Participants responding to these ads were screened over the telephone.

Recruitment numbers resulting from the study recruitment flyers and ads, and the International Pain Center are outlined in Appendix B, Tables 2 and 3 (respectively).

Study Attrition

The attrition rate in this study was high. Specifically, 64 individuals enrolled in the study; however 67.2% (43) of those who enrolled withdrew prior to completion. Additionally, study attrition appeared to be systematic. As Appendix B, Table 4 shows, completers and non-completers differed in terms of gender, with women withdrawing prior to completion more often then men. The differential gender attrition suggests that the generalizbilty of findings is questionable, and that the results with regard to gender should be interpreted with caution.

Appendix B, Table 1: Family Medicine Clinic Recruitment Efforts

Action	Quantity
Approximate number of charts reviewed*	12,200
Number of patients we tracked in an attempt to gain more information to determine eligibility and/or interest in the study (e.g. talked to the physician/nurse, talked to patient, flagged their chart to see intake results)	507
Participants consented	107
Participants qualified after consent	59
Participants completed as a result of Family Medicine clinic recruitment	17

* This is an approximate number as we did not formally track this. This number was calculated by multiplying the average number of patients seen in the clinic per day by the number of days we spent recruiting.

Appendix B, Table 2: Study Flyer and Ad Recruitment Efforts

Action	Quantity
Number of phone calls received (From March 21st to May 1st)	53
Number of individuals screened	28
Number of participants scheduled for consent	11
Number of consented participants	5
Participants completed as a result of flyers and ads	4

Appendix B, Table 3: International Pain Center Recruitment Efforts

Action	Quantity
Participants contacted	2
Participants interested and screened	0
Participants completed as a result of International Pain Center recruitment	0

Appendix B, Table 4: Study Attrition

Variable	Total Sample	Study Completers	Withdraw from Study
Total of those consented % (Count)	100% (64)	32.8% (21)	67.2% (43)
Male Sex %* (Count)	46.9% (30)	66.7% (14)	37.2% (16)
Female Sex %* (Count)	53.1% (34)	33.3% (7)	62.8% (27)
Pain Group % (Count)	60.9% (39)	66.7% (14)	58.1% (25)
Non-Pain Group % (Count)	39.1% (25)	33.3% (7)	41.9% (18)
Average Age (SD)	46.88 (10.79)	47.81 (12.06)	46.42 (10.23)

* $p < .05$, data analyzed via Chi^2 analysis

Appendix C:

Demographic Information Survey

ID: **DATE:**

Background Information

1. **Gender:** ☐ Male ☐ Female **2. Age:**_____

3. **Ethnicity:** ☐ African American ☐ Asian ☐ Caucasian ☐ Hispanic ☐ Native American ☐ Pacific Islander ☐ Other:_____

4. **Relationship Status:** ☐ Married ☐ Single ☐ Widowed ☐ Divorced ☐ Separated ☐ Cohabitating ☐ Dating ☐ Engaged

5. **Education:** Years Completed:_____
Please Check One Below:
☐ Elementary/Jr. High School ☐ Some High School ☐ GED
☐ High School Graduate ☐ Some College ☐ Associates Degree
☐ Bachelors Degree ☐ Masters Degree ☐ Doctoral Degree

6. **Employment Status:** ☐ Employed full-time ☐ Employed part-time ☐ Retired ☐ Unemployed due to pain ☐ Unemployed due to other reason ☐ Homemaker

7. **Are you on disability?** ☐ Yes ☐ No **8. Are you applying for disability?** ☐ Yes ☐ No

Health Information

9. **Height:** _____ Ft, _____ Inches **10. Weight:** _____ lbs

11. Please list all current medical conditions below:

12. Please list all current medications below (including current pain and psychiatric medications):

Medication Name	**Dose**	**How often do you take it?**	**Why is it prescribed?**
e.g. Lortab	7.5mg	2 times a day (morning & bedtime)	For pain

13. Menopausal Status (females only):
☐ Pre-Menopausal
☐ Peri-Menopausal (currently going through menopause)
☐ Post-Menopausal

14. Are you currently taking birth control (females only):
☐ Yes ☐ No
If Yes, what form of birth control do you take?:_____

15. Date of 1st day of last period (females only): _____

16. Days between 1st day of one period to the 1st day of the next: _____

17. Are your periods regular? ☐ Yes ☐ No

18. How long do your periods last (days)? _____

<u>Smoking History</u>

19. Age of first cigarette:_____ **20. Age you became a regular smoker:**_____

21. Preferred brand and type of cigarettes (current):_____

22. On average, how many cigarettes do you smoke per day (current):_____

23. How long have you been smoking at this level?:_____

24. On average, how much of a cigarette do you smoke (please check one)[1]?
☐0% ☐10% ☐20% ☐30% ☐40% ☐50% ☐60% ☐70% ☐80% ☐90% ☐100%

25. Do you Inhale[1]? ☐Always ☐Sometimes ☐Never

26. Have you ever tried to quit smoking: ☐ Yes ☐ No **27. If yes, How many times:**___

28. Month and Year of last quit attempt:_____

29. Duration of longest smoking quit attempt:_____

30. Since you began smoking regularly, what is the total amount of time in years in which you did not smoke at all?:_____

31. Are you planning to quit smoking in the next 30 days? ☐ Yes ☐ No

32. Are you planning to quit smoking in the next 6 months? ☐ Yes ☐ No

33. Is your first cigarette in the morning more satisfying than any other cigarette throughout the day? ☐ Yes ☐ No (DSM)

34. Have you ever had any of the following nicotine withdrawal symptoms (check all that apply): ☐ Low or depressed mood ☐ difficulty sleeping
☐ irritability/frustration/anger ☐ anxiety ☐ difficulty concentrating
☐ restlessness ☐ decreased heart rate ☐ increased appetite or weight gain (DSM)

35. Do you ever smoke to avoid the withdrawal symptoms listed above?
☐ Yes ☐ No (DSM)

36. Do you sometimes use up your supply of cigarettes faster than anticipated?
☐ Yes ☐ No (DSM)

37. Do you spend significant time each day acquiring cigarettes, smoking (e.g. chain smoking), or recovering from the effects of smoking? ☐ Yes ☐ No (DSM)

38. Have you been unable to cut down or quit smoking despite a desire to do so?
☐ Yes ☐ No (DSM)

39. Do you sometimes give up or reduce important social, occupational, or recreational activities because they occur in smoking restricted areas?
☐ Yes ☐ No (DSM)

40. Do you continue to smoke despite the knowledge that smoking decreases your health, has caused you health problems, or makes your health problems worse?
☐ Yes ☐ No (DSM)

41. How does smoking effect your pain (please mark one)[1]?
☐Makes pain better ☐Makes pain worse ☐No effect on pain ☐Don't Know

42. When you experience pain, do you feel the need to smoke[1]? ☐Yes ☐No

Pain History

43. Have you experienced significant constant pain over the past 6 months?
☐Yes ☐No
IF YES, Please continue. IF NO, please skip to the "Substance Use History" section.

44. Please describe what caused your pain (e.g. car accident, work related injury).

45. When did your pain begin (month and year)?_____

46. What medications have you been prescribed in the past for your pain?
47. Please list all other pain treatments you have received (e.g. surgeries, injections, acupuncture, physical therapy):

48. Do you believe that pain treatments are available for you?
☐Yes ☐No

49. Do you believe that you will spend the rest of your life with some level of pain?
☐Yes ☐No

Substance Use History

50. Have you used any of these substances in the past?

	Dates Used (e.g. 2001 to 2004)	Frequency of use (e.g. Daily)	Amount used per occasion (e.g. about 1 joint)
Amphetamine, Methamphetamine			
Marijuana (pot)			
Cocaine (crack)			
Hallucinogens (e.g. LSD, PCP, shrooms)			
Inhalants			
Opioids (e.g. heroin, vicodin, oxycontin)			

51. Do you drink beverages containing caffeine?

☐Yes ☐No

If yes, please complete the following.

	Average drinks per day? (e.g. 2 cups)	Typical serving size (e.g. 8 oz)
Coffee		
Soda (e.g. Coke)		
Tea		
Energy Drinks (e.g. Rock Star)		

Psychological History

52. Have you ever been diagnosed with a psychological or psychiatric condition (e.g. depression, anxiety, bipolar disorder, schizophrenia)?

☐Yes ☐No

If YES: please describe below

53. Have you ever been hospitalized for psychiatric or psychological reasons? If yes, please list:

Where & When	How Long	For What Reason	Outcome

Appendix D:

FTND

a) *"How soon after waking do you have your first cigarette?*
   ___Within 5 minutes (3)
   ___6-30 minutes (2)
   ___31-60 minutes (1)
   ___After 60 minutes (0)
b) *Do you find it difficult to refrain from smoking in places where it is forbidden, for example, in church, at the library, in the cinema, and so forth?*
   ___yes (1)
   ___no (0)
c) *Which cigarette would you hate most to give up?*
   ___the first one in the morning (1)
   ___any other cigarette of the day (0)
d) *How many cigarettes per day do you smoke?*
   ___10 or less (0)
   ___11-20 (1)
   ___21-30 (2)
   ___31 or more (3)
e) *Do you smoke more frequently during the first hours after waking than during the rest of the day?*
   ___yes (1)
   ___no (0)
f) *Do you smoke if you are so ill that you are in bed most of the day?*
   ___yes (1)
   ___no" (0)

FTND Score (sum of a-f):_____

Appendix E:

NWSC

Subject #_____ **Date:** _____

Session: 1 2(pre) 2(post) R1 R2

Tobacco Withdrawal Symptom Checklist

Directions: Please rate (circle) the level of your **current** withdrawal symptoms.

	NOT PRESENT	MILD	MODERATE	SEVERE
1. Craving	0	1	2	3
2. Irritability	0	1	2	3
3. Anxiety	0	1	2	3
4. Difficulty Concentrating	0	1	2	3
5. Restlessness	0	1	2	3
6. Headache	0	1	2	3
7. Drowsiness	0	1	2	3
8. Intestinal Disturbance	0	1	2	3
9. Fatigue	0	1	2	3
10. Impatience	0	1	2	3
11. Hunger	0	1	2	3
12. Insomnia	0	1	2	3

Please list any somatic (bodily) difficulties you are currently experiencing (i.e. sweating, dizziness, nausea).

1._____ 2._____

3._____ 4._____

Have you noticed any changes since your last cigarette? Yes No

If yes, what have you noticed?

_____

Appendix F:

SF-MPQ-2-A

"Now I'm going to read you a list of words that some people have used to describe the different qualities of pain and related symptoms. Using a 0 to 10 scale, with 0 meaning none at all, and 10 meaning the worst possible, I would like you to rate the intensity of each of these pain and related symptoms you have felt over the past week. Use "0" if the word does not describe your pain or related symptom."

			SF-MPQ-2											
20.	***Throbbing pain****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
21.	***Shooting pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
22.	***Stabbing pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
23.	***Sharp pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
24.	***Cramping pain****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
25.	***Gnawing pain****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
26.	***Hot-burning pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
27.	***Aching pain****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
28.	***Heavy pain****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
29.	***Tender****	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
30.	***Splitting pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
31.	***Tiring-exhausting***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
32.	***Sickening***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
33.	***Fearful***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
34.	***Punishing-cruel***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
35.	***Electric-shock pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
36.	***Cold-freezing pain***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
37.	***Piercing***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
38.	***Pain caused by light touch***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
39.	***Itching***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
40.	***Tingling or "pins and needles"***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***
41.	***Numbness***	***none***	***0***	***1***	***2***	***3***	***4***	***5***	***6***	***7***	***8***	***9***	***10***	***worst possible***

Continuous Pain: Scoring: 1+5+6+8+9+10 = raw score _____

Appendix G:

SF-MPQ-2-C

***PLEASE READ:** This questionnaire provides you with a list of words that describe some of the different qualities of pain and related symptoms. Please put an "X" through the numbers that best describe the intensity of each of the pain and related symptoms you feel right now. Use "0" if the word does not describe your pain or related symptom.*

Session: 1 2(pre) 2(post) R1 R2

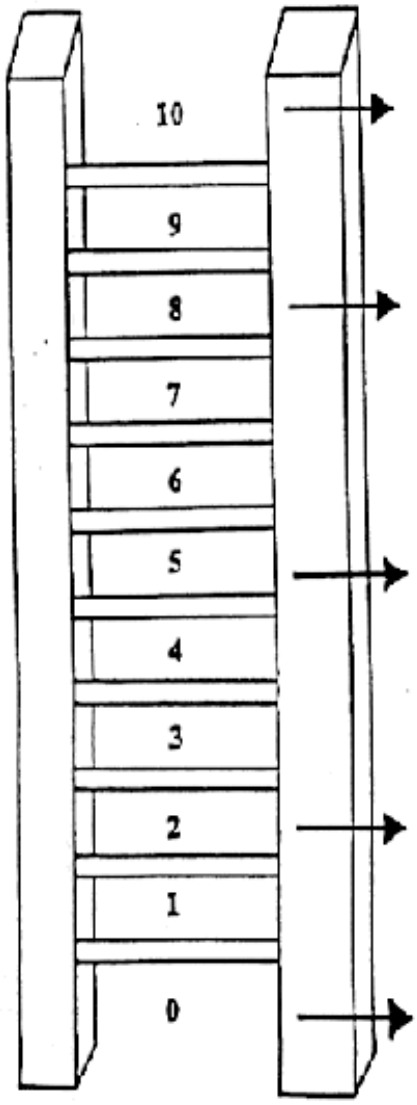
			SF-MPQ-2											
42.	**Throbbing pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
43.	**Shooting pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
44.	**Stabbing pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
45.	**Sharp pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
46.	**Cramping pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
47.	**Gnawing pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
48.	**Hot-burning pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
49.	**Aching pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
50.	**Heavy pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
51.	**Tender**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
52.	**Splitting pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
53.	**Tiring-exhausting**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
54.	**Sickening**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
55.	**Fearful**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
56.	**Punishing-cruel**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
57.	**Electric-shock pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
58.	**Cold-freezing pain**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
59.	**Piercing**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
60.	**Pain caused by light touch**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
61.	**Itching**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
62.	**Tingling or "pins and needles"**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*
63.	**Numbness**	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	*worst possible*

Appendix H:

CL

SOC – S

Each rung on this ladder represents where various cigarette smokers are in their thinking about quitting. Please circle the number that indicates where you are right now.



Taking action to quit.
(e.g., cutting down, enrolling in a program)

Starting to think about how to change my smoking patterns.

Thinking I should quit but not quite ready.

Think I need to consider quitting someday.

No thought of quitting

Appendix I:

M.I.N.I. (Example Page)

J. ALCOHOL ABUSE AND DEPENDENCE

(➡ READ QUESTIONS IN DIAGNOSTIC BOXES; CIRCLE **NO** IF "NO" AND MOVE TO THE NEXT MODULE)

		➡ NO	YES
J1	**In the past 12 months**, have you had 2 or more alcoholic drinks within a 3 hour period on 5 or more occasions?		
J2	**In the past 12 months:**		
a	Did you need to drink more in order to get the same effect that you got when you first started drinking?	NO	YES
b	When you cut down on drinking did your hands shake, did you sweat or feel agitated? Did you drink to avoid these symptoms or to avoid being hungover, for example, "the shakes", sweating or agitation? IF YES TO EITHER, CODE YES.	NO	YES
c	During the times when you drank alcohol, did you end up drinking more than you planned when you started?	NO	YES
d	Have you tried to reduce or stop drinking alcohol but failed?	NO	YES
e	On the days that you drank, did you spend substantial time recovering from drinking alcohol, drinking, or recovering from the effects of alcohol?	NO	YES
f	Did you spend less time working, enjoying hobbies, or being with others because of your drinking?	NO	YES
g	Have you continued to drink even though you knew that the drinking caused you health or mental problems?	NO	YES
	ARE 3 OR MORE J2 ANSWERS CODED YES?	NO	YES*
	* IF "NO" SKIP 12 QUESTIONS. CIRCLE "N/A" IN THE ABUSE BOX AND MOVE TO THE NEXT DISORDER. DEPENDENCE PREEMPTS ABUSE.		*ALCOHOL DEPENDENCE* **CURRENT**
J3	**In the past 12 months:**		
a	Have you been intoxicated, high, or hungover more than once when you had other responsibilities at school, at work, or at home? Did this cause any problems? (WHAT WAS USED? IF YES TO SUBSTANCE USE)	NO	YES
b	Were you intoxicated more than once in any situation where you were physically at risk, for example, driving a car, using a machine, using machinery, boating, etc.?	NO	YES
c	Did you have legal problems more than once because of your drinking, for example, arrests for disorderly conduct?	NO	YES
d	Did you go to jail or drink even though your drinking caused problems with your family or other people?	NO	YES
	ARE 1 OR MORE J3 ANSWERS CODED YES?	NO	N/A YES
			ALCOHOL ABUSE **CURRENT**

Appendix J:

Medical Record Data Collection Sheet

Date:_____ ID:_____

Current Diagnosis

Dx Date

_____
_____
_____
_____
_____
_____
_____
_____
_____
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Past Diagnosis

Dx Date

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_____
_____

Current Medications

Medication Name	Dose	Schedule	Refills

Past Medications

Medication Name	Dose	Schedule	Refills

Appendix K:

Current Medication Use Survey

ID #:_____ Date:_____

CMUS

1) Have you taken any pain medications in the past 24 hours? ☐ Yes ☐ No
If YES, please complete the following:

Medication Name	**Time(s) Taken**	**Dose**	**On a 1-10 scale, please rate how much <u>this medication</u> is decreasing your pain <u>right now</u>. (1= this medication is not helping at all, 10=I have no pain right now because of this medication)**
e.g. Lortab	8:00 last night and 7:00 this morning	7.5mg	7

2) Have you taken any other medications in the past 24 hours? ☐ Yes ☐ No
If YES, please complete the following:

Medication Name	**Time(s) Taken**	**Dose**	**Why are you taking this medication?**
e.g. Prozac	7:00 this morning	20mg	Depression

Appendix L:

Study Scripts

In-Person Script

"My name is _____, and I am part of a study investigating the relationships between chronic pain and psychological and physical factors believed to be important in the success of smoking quit attempts. Two groups of smokers will be asked to participate in this study including those who suffer from chronic pain, and those who are pain free. Each group will be asked to attend two study sessions where they will complete several surveys and provide a urine sample. Participants will also be asked to abstain from smoking for 24 hours. Following the two study sessions participants will be compensated for their time, and will receive a total of $50 for both sessions. The purpose of this study is to learn how chronic pain affects motivation to quit smoking, and the smoking abstinence experience. These are important questions, as the answers to them may affect smoking treatments are for individuals with chronic pain. Does this sound like something you would be interested in participating in?"

(if not interested…) Say: *"Thank you for your time! Have a good day."*
(if interested. . .) Say: *"Great, now I would like to go over the informed consent document"*

Go to the informed consent document. If the participant consents to participate, continue.

Go to Study Screener and Script. . . .

If participant does not qualify (based on the participation flow chart) for study say:
"Unfortunately you do not qualify for the study at this time. Thank you for your time. Have a good day."

If participant qualifies say:
"According to your answers, you qualify for the study. As I stated before, we will ask you to attend two sessions. The first study session will last about 2 ½ hours, and the second will last about 30 minutes. These study sessions will be scheduled 24 hours apart, and we will ask you to not smoke between the sessions. You will be compensated $10 after the first session and $40 after the second. Are you interested in participating?"

NO… Say: *"Thank you for your time! Have a good day."*

YES… Say: *"Great. Let's schedule your appointments. What days of the week work well for you?"*

"Will _____ on _____ work for you? The follow-up appointment will be _____ on _____. Remember, you will not be able to smoke during the 24 hours between appointments, so please plan accordingly. "

(find a time that will work, and then…)

"Great. Thank you for your time today and we will see you at _____ on _____. Please come to the Texas Tech Health Sciences Center, go into the Family Medicine Clinic, and ask for David Trotter or Katie Filtz at the front desk. Have a good day."

Study Screener and Script

1) *"How old are you?"*

Age:_____

(Must be 18 years or older to qualify)

2) *"Are you a current smoker?"*

a. ____yes ____no

(Must answer YES to qualify)

3) *"During the last 6 months, how many cigarettes do you smoke during a day?"* _____

(Must be = or > than 16 to qualify)

4) *"Have you been diagnosed with any of the following:*

a. _____*Seeing or hearing things other people don't hear*

b. _____*Mania or hypomania*

c. _____*Parkinson's Disease or Multiple Sclerosis*

d. _____*Mental retardation*

e. _____*Dementia"*

(Must say NO to all to qualify)

5) *"Are you currently experiencing regular, continuous pain?"*

a. ____yes ____no

b. ***If Yes:*** *"How long have you had that pain?"* **(please record answer)**

_____

_____

If the participant meets above criteria continue, if not say: *"Unfortunately you do not qualify for the study at this time. Thank you for your time. Have a good day."*

FTND

"Now I would like to ask you some questions about smoking"

g) *"How soon after waking do you have your first cigarette?*
   ___*Within 5 minutes (3)*
   ___*6-30 minutes (2)*
   ___*31-60 minutes (1)*
   ___*After 60 minutes (0)*

h) *Do you find it difficult to refrain from smoking in places where it is forbidden, for example, in church, at the library, in the cinema, and so forth?*
   ___*yes* (1)
   ___*no* (0)

i) *Which cigarette would you hate most to give up?*
   ___*the first one in the morning (1)*
   ___*any other cigarette of the day (0)*

j) *How many cigarettes per day do you smoke?*
   ___*10 or less (0)*
   ___*11-20 (1)*
   ___*21-30 (2)*
   ___*31 or more (3)*

k) *Do you smoke more frequently during the first hours after waking than during the rest of the day?*
   ___*yes (1)*
   ___*no (0)*

l) *Do you smoke if you are so ill that you are in bed most of the day?*
   ___*yes (1)*
   ___*no" (0)*

FTND Score (sum of a-f):_____

(Participant must score a 5 or higher on the FTND)

7) *"Now I'm going to read you a list of words that some people have used to describe the different qualities of pain and related symptoms. Using a 0 to 10 scale, with 0 meaning none at all, and 10 meaning the worst possible, I would like you to rate the intensity of each of these pain and related symptoms you have felt over the past week. Use "0" if the word does not describe your pain or related symptom."*

		SF-MPQ-2											
64. Throbbing pain*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
65. Shooting pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
66. Stabbing pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
67. Sharp pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
68. Cramping pain*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
69. Gnawing pain*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
70. Hot-burning pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
71. Aching pain*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
72. Heavy pain*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
73. Tender*	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
74. Splitting pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
75. Tiring-exhausting	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
76. Sickening	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
77. Fearful	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
78. Punishing-cruel	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
79. Electric-shock pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
80. Cold-freezing pain	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
81. Piercing	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
82. Pain caused by light touch	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
83. Itching	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
84. Tingling or "pins and needles"	none	0	1	2	3	4	5	6	7	8	9	10	worst possible
85. Numbness	none	0	1	2	3	4	5	6	7	8	9	10	worst possible

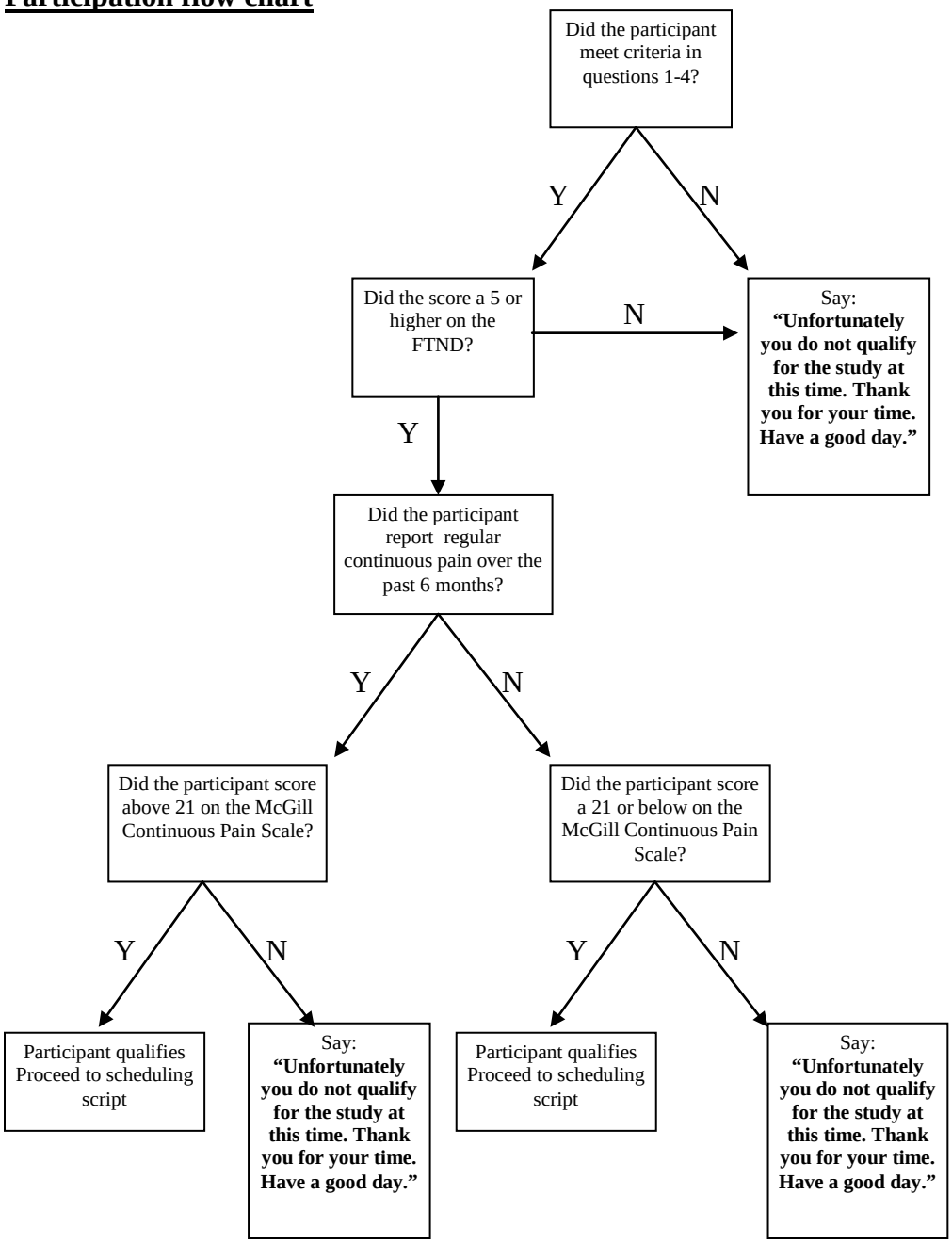
Continuous Pain: **Scoring: 1+5+6+8+9+10 = raw score** _____

Group Criteria

Non-Pain group: continuous raw score < or = 21

Pain group: continuous raw score > 21

Participation flow chart



TELEPHONE SCRIPT FOR REMINDER CALLS

If participant answers:
"Hello. My name is _____, and I am calling from Texas Tech University Health Sciences Center to remind you of your appointment on today at _____. I also want to remind you not to smoke or use any products containing nicotine during the remaining time before your appointment. Are you experiencing any difficulties abstaining from smoking? **(wait for answer)** *If you would like I can give you some strategies to help you cope with not smoking between now and your appointment."*
(if person says no, continue to closing…)
(if person says yes…)

- *"try to keep busy to keep your mind occupied, for example get together with friends and go for a walk together, read a book, listen to music you like.*
- *try chewing regular gum, ice chips, or sunflower seeds*
- *if you do get the urge to smoke, take deep breaths and remember that cravings don't usually last very long*
- *keep your hands and fingers occupied, squeeze balls, pencils, or other objects"*

CLOSING
"Thank you for your time, and we will see you later today at _____at the Family Medicine Clinic. Please ask for David Trotter or Katie Filtz at the front desk. Thank you for your participation."

If no answer:
"Hello. My name is _____, and I am calling from Texas Tech University to remind you of your appointment on today at _____, and also not to smoke or use any products containing nicotine during the remaining time before your appointment. If you need assistance or have questions please call use at 713-876-8006 or 806-368-2271. Remember, there are strategies to help you cope with not smoking listed a on a sheet given to you at your last appointment. We see you later today at _____. Thank you."

Appendix M:

Smoking Cessation Coping Handout

Coping Mechanisms For The 24-Hour Deprivation Period

- Try to keep busy to keep your mind occupied, for example:
  - get together with friends and go for a walk together
  - read a book
  - listen to music you love
  - do a crossword puzzle
- Try chewing regular gum, ice chips, sunflower seeds, etc.
- If you do get the urge to smoke, try deep breathing and remember that cravings don't usually last very long
- Keep your hands and fingers occupied, squeeze balls, pencils, or other objects