Chronic Pain Skills Study: A Preliminary Investigation
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Preface:

The Osher Center for Integrative Medicine (OCIM) at Vanderbilt is a multidisciplinary outpatient clinic treating patients with chronic pain and complex health issues via integrative services, with goals of improving overall health and wellbeing of those served. At OCIM, clinical hypnosis has been historically provided on an individual basis (by the PI, Lindsey McKernan, Ph.D). Due to its impact and increased patient demand for this service, the PI will be conducting group hypnosis services in order to expand the reach of this program. As such, we see this as a tremendous opportunity to contribute to clinical research to contribute to the evidence based for this form of service by examining patient-reported outcomes associated with participating in the treatment.

Study Schema

Significance of Research:

Results will determine if the preliminary evidence supporting the efficacy of hypnosis (HYP) in individual populations generalizes to a heterogeneous sample of VUMC patients in a group setting with chronic pain. The study findings will provide important information regarding the mechanisms of HYP, including potential moderators and mediators. If the primary study hypotheses are supported, the findings will provide the evidence needed to allow for greater access to treatments that would to reduce the pain and suffering in individuals living with chronic pain.

1.0 Background

The treatment of acute and chronic is complex and involves a variety of issues to address. Acute pain involves dramatic changes in function, is often preceded by injury, and/or may be a result of medical intervention. Reactions to these circumstances can vary but range from mild psychological distress to fear and avoidance symptoms consistent with trauma and stress-related disorders. Untreated psychological distress in response to pain can shape behavior, amplify peripheral sensations, and subsequently lead to the development of chronic pain. (1, 2). Chronic pain is a multi-faceted problem that impacts a person's physical, behavioral, emotional, and cognitive well-being (3). Additionally, a person's sense of self and future is affected, prompting major adjustments, an overhaul of one's life expectations, and often a period of grief (4).

As of yet, there is no "magic bullet" for the treatment of chronic pain. Pharmacological interventions are commonly prescribed by primary care practitioners (5, 6), yet many of these are ineffective or worse, and can be harmful to a person's health (7). Opioids have also been linked with excessive use, misuse, and death (8-10).

The need for careful consideration of opioid use has led to recent guidelines from the Centers for Disease Control and Prevention (11). While much of the emphasis in these guidelines is on proper patient selection and management with opioid medications, it is clear that the preferred option for chronic pain management is conservative intervention.

Accompanying recommendations from the CDC regarding reduced Opioid use, the most recent National Pain Strategy (2015) highlights the importance of taking an integrated, multimodal approach to managing pain in order to address the biopsychosocial factors influencing acute and chronic pain. In this model, physical disorders are considered a result of a complex and dynamic interaction among interdependent physiological, psychological, social, and environmental factors that influence the development, course, and/or resolution of illnesses (12, 13). Recommended psychological interventions generally include self-management programs, which aim to provide education and support to help patients build confidence and skills in preventing, coping

and reducing pain. Treatment is short-term in nature and has overarching goals of improving mood, increasing physical functioning, and decreasing the subjective experience of pain (14). These programs can be self-directed, integrated into health care settings, or offered by community providers (15).

One such skills-based self-management technique that may contribute to better pain management and improvements in psychological functioning and sleep quality in patients is self-hypnosis (HYP). Hypnosis is easily taught and learned, and therefore could be seamlessly incorporated into clinical practice in hospitals and clinics across the country. However, *at this point in time, little is known about the efficacy of HYP interventions for chronic pain when delivered in group settings, their effects on co-morbid conditions, and their psychological mechanisms*. Such information is critical to the development of strategies to efficiently and cost-effectively maximize their efficacy and to ensure optimal implementation.

In sum, there is a compelling need to identify additional effective treatments for individuals with chronic pain, particularly ones that offer alternatives to pharmacologic agents. One potential self-management intervention to improve pain management and symptom control is clinical hypnosis. OCIM has established hypnosis services, and is now expanding this service to include groups to increase patient access. In collaboration with Washington University School of Medicine, this project will be one of the first to examine the benefits of a formalized clinical hypnosis protocol for pain control in a group setting for patients with chronic pain.

Preliminary Studies

The scientific evidence is overwhelming that hypnosis has a positive impact in the majority of patients when used to treat both acute and chronic pain (16), showing moderate-to-large effects on pain when compared to other interventions. Through a meta-analysis of 18 studies with over 900 participants, Montgomery (2000) concluded that 75% of individuals benefit from the analgesic effects of hypnosis, demonstrating substantial pain relief regardless of the type of pain experienced, with a large effect ($d = 0.80$). A more recent meta-analysis, focusing on chronic pain only, concluded that hypnosis is efficacious and, when compared to standard care hypnosis, provided moderate treatment benefit, and a superior effect when compared to other psychological interventions for non-headache chronic pain (17). The impact of hypnosis extends far beyond pain relief – with patients reporting improved affect, relaxation, and increased energy, regardless of whether they experienced pain relief as a result of the treatment (18). This is a key finding, particularly for the treatment of chronic pain.

Studies Specific to Chronic Pain

Hypnotic approaches to chronic pain focuses on adjusting to pain, and increasing perceived control and self-efficacy, as opposed to the amelioration of pain. Hypnosis for chronic pain has been compared against treatment-as -usual, relaxation training, autogenic training, and biofeedback. It has been studied in a myriad of pain populations including headache/migraine ((19); (20)), fibromyalgia (21), advanced cancer (22), multiple sclerosis (23), and spinal cord injury (24) as examples. Large meta-analyses of these and other randomized controlled trials conclude that hypnosis is a well-established treatment for chronic pain that is efficacious, specific, and free of adverse side effects ((17); (20); (25)). There is also evidence that highly hypnotizable patients benefit from treatment to a greater degree ((26); (27); however, researchers and clinicians emphasize that most can benefit from treatment regardless, due to its ability to facilitate relaxation and because hypnotizability is not always associated with outcome (28).

Patterson and Jensen (18) concluded that there were two main findings from the accumulation of research on hypnosis for chronic pain. Firstly, the use of hypnosis can facilitate reductions in average pain intensity that, for some, can be maintained for up to 12-months. This is consistent with anecdotal reports collected from patients post-treatment, who report using self-hypnosis regularly for *temporary* pain relief (29). Essentially, hypnosis acts as a self-management tool. Secondly, the benefits of hypnosis for chronic pain extend beyond (and, in some cases, in spite of) pain relief – improving affect, relaxation, and energy levels.

Methodological Issues
While a handful of the above studies have been conducted within group settings, there are methodological issues within this research limiting their findings, which we can address through this project. Firstly, the groups evaluated have been of extremely small total sample size (i.e. ranging from 8-24 participants). In addition, the groups focused on one specific type of pain, such as back pain (McCauley et al., 1983) or pain associated with breast cancer (Elkins et al., 2004), which limits generalizability. Furthermore, many of these studies did not follow patients post-treatment to assess for maintenance of gains over time. Lastly, this study will be evaluating a specific manualized protocol developed for chronic pain patients. We believe this will extend the evidence base for hypnosis in a group format and also address the feasibility and replication of implementing a protocol in an outpatient hospital setting treating a wide range of pain disorders.

2.0 Rationale and Specific Aims

Problem Statement

Chronic pain impacts over 30 percent of the U.S. adult population, or an estimated 100 million Americans. Prevalent co-morbidities, such as substance use disorders, sleep dysregulation, mood disorders, and Post Traumatic Stress Disorder (PTSD) can amplify the experience of pain and complicate treatment.(30-32) The presence of co-morbid pain and anxiety is associated with increased service utilization(33) , decreased functionality, and higher self-reported pain, while co-morbid pain and substance use increases the risk of medication misuse.(34) Pain is also associated with greater depression and anxiety,(35) sleep dysregulation (32, 36), decreased quality of life,(37) and lower self-reported health.(38)

The most common treatments for chronic pain are analgesics.(39-41) However, chronic pain is multi-dimensional in nature and is therefore often refractory to these and other biomedical interventions.(42) Moreover, the most powerful analgesics – opioids – are associated with adverse side effects including sedation, constipation, and respiratory depression. More specifically, they are potentially addictive, which can contribute to their misuse, addiction, and diversion (e.g., selling, hoarding or non-prescribed use).(43) Further, opioid analgesics typically engender tolerance effects.

Several chronic pain self-management approaches have been developed that provide patients with a skill-set they can use – anywhere and anytime – to better manage pain and its effects on their lives. Importantly, these treatments encourage individuals to play an active role in their healthcare, rather than remain a passive recipient of biomedical interventions. Despite evidence to support team- based, pain self-management programs for pain, their implementation has lagged, which represents an unmet opportunity to provide people with pain the appropriate skills, education, and resources to play an active role in managing their pain.

One skills-based self-management technique that may contribute to better pain management and improvements in psychological functioning and sleep quality in patients is self-hypnosis (HYP). Hypnosis is easily taught and learned, and therefore could be seamlessly incorporated into clinical practice in hospitals and clinics across the country. However, *at this point in time, little is known about the efficacy of HYP interventions for chronic pain when delivered in group settings, their effects on co-morbid conditions, and their psychological mechanisms*. Such information is critical to the development of strategies to efficiently and cost-effectively maximize their efficacy and to ensure optimal implementation.

The purpose of this pilot project is to test the efficacy and mechanisms of HYP on chronic pain in up to 105 Patients. Primary (characteristic pain intensity) and secondary (mood, quality of life) outcomes will be assessed at pre-treatment, three times during treatment, post-treatment, and at 3- and 6-month follow-up. Potential treatment moderators and mediators will also be assessed. The study will address two aims:

Aim 1: Determine the efficacy of 8 sessions of group delivered HYP training for reducing characteristic pain intensity in patients. The hypothesis associated with Aim 1 is:

Hypothesis 1: *Primary Study Hypothesis*. Patients receiving 8 sessions of HYP training will report significantly reduced pre- to post-treatment decreases in average pain intensity.

Aim 2 : To evaluate potential moderators (hypnotizability) **associated with treatment outcomes following intervention**. The hypothesis associated with Aim 2 is:

Hypothesis 2a: Hypnotizability will augment treatment outcomes such that those with higher hypnotizability will experience significantly greater treatment gains.

In addition to testing the above specific hypotheses, we will use the data obtained in this study to further explore (1) the longer-term (up to 6 months) effects of HYP and (2) additional potential moderators (e.g., treatment outcome expectancies, treatment motivation, demographic variables, pain type [neuropathic vs. nociceptive]) and mediators (pain acceptance, catastrophizing, mindfulness, therapeutic alliance, amount of skill practice between sessions) of treatment outcome. We intend to later expand this study to include a measure of biological mechanisms, using this data to apply for a larger, more rigorous trial (i.e. RO1).

3.0 Inclusion/Exclusion Criteria

Participants:
We propose to enroll 105 participants in order to ensure complete data from 60 participants, assuming approximately a very conservative 45% drop-out rate (the dropout rate in other associated studies has ranged from 12-30%). We will monitor the dropout rate on an ongoing basis, and modify the number of participants recruited as needed to ensure a final sample of N = 60 study completers.

Inclusion Criteria:

(1) 18 years of age or older; *
(2) Self-reported presence of chronic pain;**
(3) Average pain intensity rating of ≥ 3 on a 0-10 Numerical Rating Scale (NRS) of pain intensity in the last week; **
(4) Worst pain intensity rating of ≥ 5 on a 0-10 Numerical Rating Scale (NRS) of pain intensity in the last week;**
(5) Duration of chronic pain 3 months or more; **
(6) Experiences pain at least 75% of the time in the past 3 months; Those who have a hard time answering this question will be asked the following question: "Which statement best describes your pain?"
    (a) Pain all the time, but the pain intensity varies;
    (b) Pain most of the time with only occasional periods of being pain-free;
    (c) Pain that comes and goes;
    (d) Occasional pain;

    Participants must report experiencing pain that matches one of the first two options;**
(7) Able to read, speak, and understand English.**

Exclusion Criteria:

(1) Cognitive impairment or limitations (i.e. history of moderate to severe TBI, unresolved TBI, or other medical condition) that would interfere with a patient's ability to participate in a group involving focused attention*.
(2) Current or history of diagnosis of primary psychotic or major thought disorder as listed in participant's medical record or self-reported within the past five years;*
(3) Hospitalization for psychiatric reasons other than suicidal ideation, homicidal ideation, and/or PTSD self-reported or noted in chart (within the past 5 years);*
(4) Psychiatric or behavioral conditions in which symptoms are unstable or severe (e.g. current delirium, mania, psychosis, suicidal ideation, homicidal ideation, substance abuse dependency) as listed in participant's medical record or self-reported within the past six months;*
(5) Any behavioral issues as noted in the medical record that would indicate the participant may be inappropriate in a group setting;***
(6) Presenting symptoms at time of screening that would interfere with participation, specifically active suicidal ideation with intent to harm oneself or active delusional or psychotic thinking;**
(7) Difficulties or limitations communicating over the telephone;**
(8) Any planned life events that would interfere with participating in the key elements of the study.**
(9) Reported average daily use of >120mg morphine equivalent dose (MED). **

*also verified via medical record review, as described below.
**verified solely via self-report, as described below; there is no medical record review component.
***verified solely via medical record review, there is no self-report component.

There will not be an upper age cutoff for study participation because individuals of all ages can be successfully treated, including those over 80 years old. Moreover, age is one of the potential moderator variables we propose to study, so we will be better able to evaluate age effects with greater age variability in the sample.

4.0 Enrollment

The registration process will occur at the Osher Center for Integrative Medicine at Vanderbilt, located at 3401 West End Avenue, Suite 380, Nashville, TN 37203, or following telephone screening for the study outside of OCIM. Following study screening, the assessment measures will be completed via computer on-site at OCIM or online through a secure RedCap link. There is no randomization process for this study.

Recruitment

Individuals referred to group hypnosis for pain control at the Osher Center for Integrative Medicine at Vanderbilt (OCIM) will be recruited for potential inclusion in this research study. Referrals to the group hypnosis program at OCIM generally occur in one of three ways: 1) internally within OCIM, 2) through another provider at VUMC, and 3) self-referral. Participants will be made aware of group services available in clinic through word-of-mouth, rotating information posted in waiting rooms regarding group offerings and timetables, and through discussion with providers. In addition, flyers and information regarding this service may be posted at additional outpatient clinics at VUMC per usual practice.

Due to the popularity of this service at OCIM and long waiting list for hypnosis treatment, we do not anticipate having to expand recruitment beyond clinical practice as usual.

Screening Procedures

All patients referred to services at OCIM are seen by a provider first-hand in order to establish an integrative treatment plan as a part of their treatment.

During this medical appointment, individuals interested in clinical hypnosis will complete a "Hypnosis Referral Form" (attached) with their provider. This form will either be completed on paper or via electronic health record once available as a part of standard clinical practice. This form assesses for the presence of chronic pain, current pain intensity, and appropriateness for group. This form will serve as a screening procedure for group involvement and potential research participation, as the criteria for being in the group are the same as for those wishing to participate in research. On this referral form, the potential participant will also indicate their willingness to participate in the research associated with the hypnosis group. In the event that a medical provider is unable to screen potential group participants prior to their inclusion in the group, the PI or group facilitator will contact the participant and ask the questions on the "Hypnosis Referral Form" via telephone.

Screening Procedures, non-research participants

Screening procedures for non-research participants will be identical to those who may be interested in research. Those who indicate that they do not wish to participate in the research aspect of the clinical service or have chronic pain but do not meet inclusion criteria for the study (e.g. pain is occasional or sporadic, or daily pain is not greater that 3/10 on NRS) will either 1) not be approached with research information or 2) informed of their inability to participate in the research but still offered the clinical service.

5.0 Study Procedures

Pre-treatment Assessments

Those who indicate they are interested in participating in research during screening procedures and meet inclusion criteria will be contacted by the PI or a member of the research team (e.g. project coordinator, post-doctoral fellow, or research assistant) to discuss study procedures, answer any questions, and confirm dates/times of the group. This will occur via telephone or in-clinic if a member of the research team is available. Those who wish to enroll in the study will be emailed an informed consent and link to pre-treatment assessments in RedCap. If the enrollee does not have computer access, has not completed assessments online prior to group starting, or prefers paper-and-pencil measures, a computer will be available in the waiting room area for use to complete this paperwork or a hard copy of the assessment packet will be available for the participant to complete in clinic. This process has been implemented within OCIM for intake procedures and is already established as a clinical procedure. As such, we expect the implementation of online/computer-based and in-clinic assessments to be feasible. Please refer to Table 1 for a list of measurements and timeline of their administration.

Treatment Phase

Group hypnosis appointments will be scheduled in regular group clinics at OCIM at Vanderbilt, 3401 West End Avenue, Suite 380, Nashville, TN 37203. Treatment sessions will appear on participant's lists of regular clinical appointments. Although the appointments are scheduled for 90 minutes, in practice they will last 60-80 minutes, with a 10 minute time cushion built in to allow for participants who may have mobility limitations to arrive, settle, and then vacate the group rooms without hurrying. The reason that there is variation in the amount of time planned for each group (60-80 minutes) is that some of the sessions may require more time than others; for example, the first session will take more time than the others because it will include time for introductions and reviewing the format of the treatment, as well as for answering questions about treatment. Some groups may have participants with mobility limitations who require a little longer than others to get physically settled into the room, some may require a 5-10 minute break during the session, and some groups- especially those

with higher numbers of participants- may require a little more time than others to ensure each participant has an opportunity to actively participate and discuss.

The group sessions will be initially conducted by the PI and a post-doctoral fellow in Psychology. If the service expands, groups will also be conducted by OCIM/VUMC providers who are competent in practicing clinical hypnosis and/or have undergone a formal two-day training process that prepares clinicians to conduct the intervention in a group setting. Potential providers will be licensed/credentialed/privileged allied health professionals or providers-in-training under supervision from a licensed professional from the following disciplines: Ph.D. licensed Psychologists, advanced Clinical Psychology Doctoral Candidates under the supervision of the PI, Pre-doctoral Clinical Psychology Interns (i.e., who are in their final year of a doctoral degree program and supervised by a licensed Clinical Psychologist) and Psychology Post-doctoral Fellows (who have completed a Ph.D.), Psychiatry Residents, Physical Therapists (PT, DPT), or Nurses (RN). Each provider will participate in a two-day training, which will cover group instruction for self-hypnosis. All study clinicians will also be given regular feedback by the PI (Dr. McKernan) on their performance. In addition, ongoing consultation will be offered to providers leading self-hypnosis interventions by Dr. McKernan to ensure that any questions that in real time can be answered.

Each group will be led by two providers allowing for groups to continue as scheduled in the event one of the providers is unable to attend a particular group. Groups will be scheduled to start when at least ten participants are enrolled.

Additional participants will be scheduled for the groups until they reach the maximum size of fifteen. Providers will be expected to follow closely the treatment manuals to ensure all scheduled material is covered, and to ensure the consistency and replicability of treatment.

Self-hypnosis home practice activities will be assigned to increase engagement in the treatment. Participants will be asked to record the extent of engagement in these activities using a form provided to them by the clinician. We realize that adherence to interventions assigned outside of treatment sessions may influence study outcomes so will utilize data collected by the clinicians about homework compliance. In addition, all participants in all interventions will be given a treatment workbook with materials to refer to and discuss during the group sessions as well as additional materials to read between sessions.

HYP treatment. In the HYP treatment, each group session will be highly structured. Group sessions will begin with a review and discussion of the home practice assignments and goals for the session. The facilitator will preform a standard hypnotic short induction followed by therapeutic suggestions, including post-hypnotic suggestions.

Participants will relax in a comfortable position with their eyes closed and will simply listen to the clinician read a standardized hypnotic script that will include an induction followed by suggestions for decreased pain and improvement in co-morbid symptoms (e.g., improved mood and optimism, relaxation, sleep quality). Sessions will also include discussion post-exercise. The sessions will end with recommendations for home practice. Participants will be given pre-recorded recordings of the hypnotic inductions and suggestions provided in each session and encouraged to practice self-hypnosis (first, using recordings, but over time and as they gain more confidence, on their own without the recordings), and time will be devoted to problem solving around any difficulties with self-hypnosis practice. The PI has a great deal of experience with this intervention, conducting hypnosis for pain for over 6 years. The PI has also been utilizing this intervention at OCIM for two years on an individual basis.

Timetable: Once patients are screened and determined to be eligible to participate in the study, they will complete informed consent and an assessment battery online or via computer on-site at OCIM either the same day or returning on a separate day, if requested. They will then be enrolled in the next group series, which we anticipate to occur roughly every two months. With groups occurring 5 times per year with 15 participants, we anticipate a study inclusion rate of 75%. In order to recruit 105 participants with a conservative estimated dropout rate of 45%, including follow-up we anticipate this study will occur over the course of two years.

Measures Used

General Information

Demographics: Patients will complete an 12-item brief demographic questionnaire indicating age, gender, race, religious orientation, and household income. Patients will also indicate their diagnoses and information regarding diagnosis/treatment. The questionnaire will take approximately 3 minutes to complete.

Expectancy Questionnaire: Participants will be asked open-ended questions to assess their expectancies and in order to provide qualitative feedback regarding the impact of treatment on their life, health, and functioning. The questions range from a single question to six questions, depending on what timeframe the participant is being assessed.

Pain and Physical Functioning

PainDetect (PD-Q; (44)) is a simple, patient-based, easy to use screening tool to assess the presence of neuropathic and nociceptive pain. It consists of 9 self-report items that assess for the quality, spatial characteristic, and individual pain patterns. It takes roughly 1-2 minutes to complete.

Brief Pain Inventory (severity scale only; (45)) is a 4-item subscale of the Brief Pain Inventory assessing the severity of pain over the past week. Questions inquire into an individual's worst, least, average, and current levels of pain on an 11-point likert scale. It has been validated and is considered the gold standard to utilize in patient-reported outcomes studies (46). It takes <1 minute to complete.

PROMIS Pain Interference (47) – The Patient-Reported Outcomes Measurement Information System® (PROMIS®) was designed to develop, validate, and standardize item banks to measure key domains of physical, mental, and social health in chronic conditions. The PROMIS Pain Interference is a 6 item likert-scale questionnaire measuring the self-reported consequences of pain on relevant aspects of a person's life including its impact on social, cognitive, emotional, physical, and recreational activities. It has been developed by experts for use in clinical trials and validated across populations. It takes <1 minute to complete.

Michigan Body Map: The Michigan Body Map (48) is a self-report measure used to assess the location(s) of chronic pain complaints and widespread body pain. It is a one-sided body image with check-box responses for 35 potential body areas where chronic pain (defined as pain > 3 months) might exist, and a box for "no pain." It takes 2-3 minutes to complete. In this study, the measure is being used as an indication of centralized pain and pain sensitivity.

Emotional Functioning

The Pain Catastophizing Scale (PCS; (49)) is a 13 item self-report questionnaire evaluating thoughts and feelings associated with pain experiences. On this scale, respondents indicate from 0 ("not at all") to 4 ("all the time") the frequency with which they experience different thoughts and feeling associated with pain. The measure takes roughly 2-3 minutes to complete. It is well-known, reliable, and valid measure assessing pain-related catastrophic thinking (50).

PROMIS Emotional Distress Scales (51): The Patient-Reported Outcomes Measurement Information System® (PROMIS®) was designed to develop, validate, and standardize item banks to measure key domains of physical, mental, and social health in chronic conditions.The PROMIS emotional distress scales ask about specific symptoms related to depression and anxiety and the degree to which a person has felt that symptom on a likert scale within the past week. For this investigation we will be using the short-form of the Anxiety and

Depression subscales only. They are 8 items each, respectively. These scales been developed by experts for use in clinical trials and validated across populations. They will take approximately 2 minutes to complete.

PROMIS Self-Efficacy for managing symptoms(52): The Patient-Reported Outcomes Measurement Information System® (PROMIS®) was designed to develop, validate, and standardize item banks to measure key domains of physical, mental, and social health in chronic conditions. The self-efficacy for managing symptoms is an 8-item questionnaire on a likert scale that assesses a person's perceptions of his/her ability to exercise self-care in the face of illness. It takes approximately 1 minute to complete.

PROMIS Global Health: The Patient-Reported Outcomes Measurement Information System® (PROMIS®) was designed to develop, validate, and standardize item banks to measure key domains of physical, mental, and social health in chronic conditions. We will be using a subscale assessing overall quality of life as a result of symptoms. This is a single item question that asks patients to rate their overall quality of their health on a 5-point likert scale ranging from "poor" to "excellent."

Patient Global Impression of Improvement (PGI): The PGI is a global index used to rate the response of a condition to an intervention. Patients rate their impression of change on a 7-point likert scale ranging from "very much improved" to "very much worse." This question is routinely used in clinical care and has been validated as a tool to assess perceived impact of disease management (53). This questionnaire will be given post-treatment and at follow-up only.

Hypnotizability
The Harvard Group Scale of Hypnotic Susceptability (HGSHS (54)) is a standardized hypnotic procedure assessing a participant's responsiveness to hypnosis. This scale consists of a hypnosis induction followed by a series of 12 suggestions

Optional Questionnaires
Fibromyalgia Impact Questionnaire (FIQ-R (55); to be given to patients with or suspected of having Fibromyalgia only): is a self-report tool designed to measure the impact of Fibromyalgia symptoms on overall functioning and quality of life. It has been validated and is widely used as an outcome measure in clinical trials. It consists of 21 individual questions based on an 11-point numeric rating scale of 0-10 with 10 being "worst." All questions are framed within the context of the past week. The FIQ-R takes approximately 1-2 minutes to complete.

American Urological Association Symptom Index (AUASI; to be given to participants with Urologic symptoms only (56)) is based on the answers to seven questions concerning urinary symptoms and one question concerning quality of life. Each question concerning urinary symptoms allows the patient to choose one out of six answers indicating increasing severity of the particular symptom. The answers are assigned points from 0 to 5. The total score can therefore range from 0 to 35 (asymptomatic to very symptomatic). It is widely used and reliable measure of lower urinary tract symptoms. It takes approximately 2 minutes to complete.

Data Collection & Management
Attendance Recording
Group leaders (clinicians) will be given an attendance record of the anticipated participants in their group and will be responsible for ensuring scheduling and other clinical matters are managed once the groups start. The attendance record will only include a participant's name and MRN. This will be confirmed by a member of the research team. The clinician will record the subject's absence or presence for each session on the record.

Completed attendance records will be uploaded and stored on a limited access folder on the secure VUMC network drive. Only Dr. McKernan and members of the research team will have access to this drive. The hard copies of these attendance records will be destroyed once they are uploaded to the drive at the end of each treatment group.

Data Collected during Treatment Sessions
Participants will complete and hand in a form regarding their completion of tasks or "homework" assigned by the clinician from the previous session.

In addition, participants will complete and hand in forms before and after each session that include questions regarding pain intensity and comfort level, as well as questions about what the participants have found helpful or non-helpful about the treatment.
Finally, study clinicians will complete a form each session that captures information regarding the perceived engagement of each participant in that particular session. All of these forms will be labeled with a subject's name.

Information will be gathered during the group interventions as per standard of care procedures that all attendees will do regardless of their participation in the study. The clinicians running the groups will not administer any activities that fall outside of the realm of standard care. Following each session, per usual care the clinician will enter a progress note in Starpanel for each participant present at that particular session. The note will also include the length of the group session, as well as basic content covered during the session and pain ratings obtained during the session (standard care). Information gathered during the group sessions (e.g., homework logs, pre- and post-class pain ratings, patient engagement) will also be used for clinical supervision and treatment planning.

Once utilized for standard care purposes (e.g. note writing, clinical supervision), information collected on non-research participants on paper (e.g. data collected during treatment sessions) will be destroyed. Information collected on research participants will be stored in a password protected database on a secure VUMC server only accessible to the PI and members of the research team. We will do this by first confirming the participant's subject number, indicating this on the paper document, de-identifying any personal information, and uploading the file as a PDF into a separate file on a secure, password protected drive. This information will also be recorded into RedCap by a member of the research team.

Post-treatment Assessments & Hypnotizability Assessment
Participants will complete assessments immediately post-treatment, 3-months, and 6-months post-treatment. These assessments are listed in Table 1 and participants will be invited to complete them via RedCap, on paper or computer in clinic at OCIM, or will be mailed follow-up assessments with a stamped return envelope as needed. Immediately post-treatment, participants will also be asked to return to clinic the following week to complete an assessment of hypnotizability using a standardized scale (HGSHS, (54)). For the 3 and 6 month follow-up phase, participants will be contacted via email and/or telephone (using a script) to be reminded of their need to complete assessments and either complete these online, in clinic, or be mailed follow-up assessments.

Compensation:
Participants will be compensated $10 for pre, post, and follow-up assessments ($40 total). This compensation will be paid in the form of gift cards from Target, Starbucks, or Amazon.com. These funds will be given either from Vanderbilt's VICTR CTSA voucher program (#52095), through limited research funds of the PI, or through the Vanderbilt Osher Center for Integrative Medicine endowment.

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

In accordance with federal regulations and VUMC policy, adverse events and unanticipated problems involving risk to participants or others that fall under VUMC IRB jurisdiction will be reported to the VUMC IRB within 10 working days after learning of the event or problem.

7.0 Study Withdrawal/Discontinuation

Treatment Withdrawal

Participants may withdraw from the study at any time without loss of payment. Individuals may be withdrawn from the study if the PI learns that a participant does not meet study inclusion criteria after assessments have been completed. These participants will still be offered the clinical service. If this occurs, the data will not be recorded into the database and the participant will be withdrawn from the sample.

Treatment Intervention Discontinuation

As per standard clinical procedures, a participant will be withdrawn from the treatment intervention if s/he (1) engages in behavior that is disruptive to the group, and/or (2) engages in behavior that interferes with the appropriate administration of the group treatment.

However, participants who are withdrawn from the study treatment intervention will be invited to complete study assessments during treatment, post-treatment, 3-month and 6-month follow-up in order to allow for complete data for the planned intent-to-treat analyses. Participants will receive payment for the time it takes to provide outcome data at each assessment point.

8.0 Statistical Considerations

The hypotheses outlined above will be tested through bivariate correlation, t-tests, and repeated-measures regression analyses. Specifically, relationships among variables of interest (Hypotheses 1) will be assessed through Pearson product-moment correlation analyses to determine the strength of the association among these constructs in our sample and a repeated measures ANOVA to assess change in the primary outcome measure (NRS pain intensity) pre and post-treatment. Tests of moderation (Hypotheses 2) will be tested using multiple linear regression with cross-products of the variables of interest to assess the interaction between predictors. All analyses will be carried out on either SPSS 22 (IBM, 2013) or the R statistical package (57)

9.0 Privacy/Confidentiality Issues

Minimization of risk: As per standard clinical care, potential group participants will be screened by an OCIM medical or behavioral health provider prior to enrollment utilizing the hypnosis referral form. Participants in any acute emotional distress, with cognitive limitations, or considered to be unstable behaviorally or psychologically will not be referred to group.

Informed consent will be obtained electronically or on paper (if assessments completed in clinic) for each participant in the study prior to their participation. Assessment data will be entered and stored using RedCap/SPSS in encrypted files on an encrypted laptop computer belonging to the PI. Participant tracking information will be stored on a separate password-protected excel file only accessible to the PI and a research team member. Paper assessments will be entered into Redcap by a member of the research team and de-identified following completion. They will be given a unique number, with tracking information of this number only accessible to the PI and members of the research team. Consent forms completed on paper will be stored in a separate file in a locked cabinet. A limited data set, containing no identifying information, may be shared

with collaborating individuals at regional institutions. Such individuals will have signed Data Use Agreements with VUMC and will abide by these contracts prior to having access to any such information.

The proposed study design involves non-invasive procedures. The data described other than the data collected during the group treatment sessions will be collected solely for research purposes (e.g. assessments, medical record data, demographics). Participants will be informed that data collected before and after treatment sessions, i.e. data regarding homework practice, pain intensity and comfort before and after each treatment session, and participant engagement as per the study clinician, will be reported in their medical record, as clinically indicated. Research participation will not influence any part of a patient's medical treatment.

10.0 Follow-up and Record Retention

The study duration is estimated at 24 months. Data will be stored for five years after publication in de-identified form and informed consent forms will be kept for 3 years as per federal law. All data will be stored electronically where available and paper assessments and consent forms will be stored in separate locked filing cabinets on site at OCIM. Information collected in databases may be archived indefinitely to support future research efforts.

References

1. Norton PJ, Asmundson GJG. Amending the fear-avoidance model of chronci pain: What is the role of physiological arousal? Behavior Therapy. 2003;34(1):17-30.
2. Vlaeyen JW, Linton SJ. Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art. Pain. 2000;85(3):317-32.
3. Institute of Medicine (U.S.). Committee on Advancing Pain Research Care and Education. Relieving pain in America : a blueprint for transforming prevention, care, education, and research. Washington, D.C.: National Academies Press; 2011. xvii, 364 p. p.
4. Morley S. Psychology of pain. British journal of anaesthesia. 2008;101(1):25-31.
5. Mafi JN, McCarthy EP, Davis RB, Landon BE. Worsening trends in the management and treatment of back pain. JAMA Intern Med. 2013;173(17):1573-81.
6. Jeffrey Kao MC, Minh LC, Huang GY, Mitra R, Smuck M. Trends in ambulatory physician opioid prescription in the United States, 1997-2009. PM R. 2014;6(7):575-82 e4.
7. Abdel Shaheed C, Maher CG, Williams KA, Day R, McLachlan AJ. Efficacy, Tolerability, and Dose-Dependent Effects of Opioid Analgesics for Low Back Pain: A Systematic Review and Meta-analysis. JAMA Intern Med. 2016;176(7):958-68.
8. Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, et al. The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. Annu Rev Public Health. 2015;36:559-74.
9. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths--United States, 2000-2014. MMWR Morb Mortal Wkly Rep. 2016;64(50-51):1378-82.
10. Kenan K, Mack K, Paulozzi L. Trends in prescriptions for oxycodone and other commonly used opioids in the United States, 2000-2010. Open Med. 2012;6(2):e41-7.
11. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain--United States, 2016. JAMA. 2016;315(15):1624-45.

12. Turk DC, In DC. A cognitive-behavioral perspective on treatment of chronic pain patients. Turk RJ Gatchel Eds Psychological Approaches to Pain Management A practitioners guide p London Guilford Press. 2002:138-58
SRC - GoogleScholar.
13. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC. The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychological bulletin. 2007;133(4):581.
14. Williams DA, In DJ, Philadelphia PA. Cognitive and behavioral approaches to chronic pain. Wallace DJ Clauw Eds Fibromyalgia and other central pain syndromes p Lippincott Williams Wilkins. 2005:343-52
.
15. Department of Health and Human Services. National Pain Strategy: A Comprehensive Population Health Strategy for Pain. 2015.
16. Patterson DR. Clinical Hypnosis for Pain Control. Washington, DC: American Psychological Association; 2010. 275 p.
17. Adachi T, Fujino H, Nakae A, Mashimo T, Sasaki J. A meta-analysis of hypnosis for chronic pain problems: A comparison between hypnosis, standard care, and other psychological interventions. International Journal of Clinical and Experimental Hypnosis. 2014;62(1):1-28.
18. Jensen MP, Patterson DR. Hypnotic approaches for chronic pain management: clinical implications of recent research findings. American Psychological Association. 2014;69(2):167-77.
19. Spinhoven P, Linssen AC, Van Dyck R, Zitman FG. Autogenic training and self-hypnosis in the control of tension headache. General Hospital Psychiatry. 1992;14(6):408-15.
20. Hammond DC. Review of the efficacy of clinical hypnosis with headaches and migraines. International Journal of Clinical and Experimental Hypnosis. 2007;55(2):207-19.
21. Castel A, Perez M, Sala J, Padrol A, Rull M. Effect of hypnotic suggestion on fibromyalgic pain: comparison between hypnosis and relaxation. European Journal of Pain. 2007;11(4):463-8.
22. Elkins G, Marcus J, Palamara L, Stearns V. Can hypnosis reduce hot flashes in breast cancer survivors? A literature review. American Journal of Clinical Hypnosis. 2004;47(1):29-42.
23. Jensen MP, Barber J, Romano JM, Molton IR, Raichle KA, Osborne TL, et al. A comparison of self-hypnosis versus progressive muscle relaxation in patients with multiple sclerosis and chronic pain. International Journal of Clinical and Experimental Hypnosis. 2009;57(2):198-221.
24. Jensen MP, Barber J, Romano JM, Hanley MA, Raichle KA, Molton IR, et al. Effects of self-hypnosis training and EMG biofeedback relaxation training on chronic pain in persons with spinal-cord injury. International Journal of Clinical and Experimental Hypnosis. 2009;57(3):239-68.
25. Montgomery GH, DuHamel KN, Redd WH. A meta-analysis of hypnotically induced analgesia: how effective is hypnosis? International Journal of Clinical and Experimental Hypnosis. 2000;48(2):138-53.
26. Gay MC, Philippot P, Luminet O. Differential effectiveness of psychological interventions for reducing osteoarthritis pain: a comparison of Erikson [correction of Erickson] hypnosis and Jacobson relaxation. European Journal of Pain. 2002;6(1):1-16.
27. Ter Kuile MM, Spinhoven P, Linssen AC, Zitman FG, Van Dyck R, Rooijmans HG. Autogenic training and cognitive self-hypnosis for the treatment of recurrent headaches in three different subject groups. Pain. 1994;58(3):331-40.
28. Jensen MP, Hanley MA, Engel JM, Romano JM, Barber J, Cardenas DD, et al. Hypnotic analgesia for chronic pain in persons with disabilities: a case series. International Journal of Clinical and Experimental Hypnosis. 2005;53(2):198-228.
29. Jensen MP, McArthur KD, Barber J, Hanley MA, Engel JM, Romano JM, et al. Satisfaction with, and the beneficial side effects of, hypnotic analgesia. International Journal of Clinical and Experimental Hypnosis. 2006;54(4):432-47.
30. Morasco BJ, Lovejoy TI, Lu M, Turk DC, Lewis L, Dobscha SK. The relationship between PTSD and chronic pain: mediating role of coping strategies and depression. Pain. 2013;154(4):609-16.

31. Lang KP, Veazey-Morris K, Andrasik F. Exploring the Role of Insomnia in the Relation Between PTSD and Pain in Veterans With Polytrauma Injuries. J Head Trauma Rehabil. 2013.
32. Wallace DM, Shafazand S, Ramos AR, Carvalho DZ, Gardener H, Lorenzo D, et al. Insomnia characteristics and clinical correlates in Operation Enduring Freedom/Operation Iraqi Freedom veterans with post-traumatic stress disorder and mild traumatic brain injury: an exploratory study. Sleep Med. 2011;12(9):850-9.
33. Beehler GP, Rodrigues AE, Mercurio-Riley D, Dunn AS. Primary Care Utilization among Veterans with Chronic Musculoskeletal Pain: A Retrospective Chart Review. Pain Medicine. 2013;14(7):1021-31.
34. Morasco BJ, Dobscha SK. Prescription medication misuse and substance use disorder in VA primary care patients with chronic pain. General Hospital Psychiatry. 2008;30(2):93-9.
35. Patton CM, Hung M, Lawrence BD, Patel AA, Woodbury AM, Brodke DS, et al. Psychological distress in a Department of Veterans Affairs spine patient population. Spine J. 2012;12(9):798-803.
36. Tan G, Teo I, Srivastava D, Smith D, Smith SL, Williams W, et al. Improving access to care for women veterans suffering from chronic pain and depression associated with trauma. Pain Medicine. 2013;14(7):1010-20.
37. Bras M, Milunovic V, Boban M, Brajkovic L, Benkovic V, Dordevic V, et al. Quality of life in Croatian Homeland war (1991-1995) veterans who suffer from post-traumatic stress disorder and chronic pain. Health Qual Life Outcomes. 2011;9:56.
38. Forman-Hoffman VL, Peloso PM, Black DW, Woolson RF, Letuchy EM, Doebbeling BN. Chronic widespread pain in veterans of the first Gulf War: impact of deployment status and associated health effects. Journal of Pain. 2007;8(12):954-61.
39. Pollmann W, Feneberg W. Current management of pain associated with multiple sclerosis. CNS Drugs. 2008;22(4):291-324.
40. Wasner G. Central Pain Syndromes. Current Pain and Headache Reports. 2010.
41. Solaro C, Messmer Uccelli M. Pharmacological management of pain in patients with multiple sclerosis. Drugs. 2010;70(10):1245-54.
42. Baastrup C, Finnerup NB. Pharmacological management of neuropathic pain following spinal cord injury. CNS Drugs. 2008;22(6):455-75.
43. Trescot AM, Glaser SE, Hansen H, Benyamin R, Patel S, Manchikanti L. Effectiveness of opioids in the treatment of chronic non-cancer pain. Pain Physician. 2008;11(2 Suppl):S181-200.
44. Freynhagen R, Baron R, Gockel U, Tolle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Current medical research and opinion. 2006;22(10):1911-20.
45. Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. The Clinical journal of pain. 2004;20(5):309-18.
46. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain. 2005;113(1–2):9-19.
47. Amtmann D, Cook KF, Jensen MP, Chen WH, Choi S, Revicki D, et al. Development of a PROMIS item bank to measure pain interference. Pain. 2010;150(1):173-82.
48. Brummett CM, Hassett AL, Brummett KA, Clauw DJ, Williams DA. The Michigan Body Map and its use in assessing the American College of Rheumatology survey criteria for Fibromyalgia
. Arthritis & Rheumatism. 2011;62:744.
49. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. Psychological assessment. 1995;7(4):524.
50. Osman A, Barrios FX, Kopper BA, Hauptmann W, Jones J, O'Neill E. Factor structure, reliability, and validity of the Pain Catastrophizing Scale. Journal of behavioral medicine. 1997;20(6):589-605.

51. Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D. Item Banks for Measuring Emotional Distress From the Patient-Reported Outcomes Measurement Information System (PROMIS®): Depression, Anxiety, and Anger. Assessment. 2011;18(3):263-83.
52. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): Progress of an NIH Roadmap Cooperative Group During its First Two Years. Medical care. 2007;45(5 Suppl 1):S3-S11.
53. Rampakakis E, Ste-Marie PA, Sampalis JS, Karellis A, Shir Y, Fitzcharles M-A. Real-life assessment of the validity of patient global impression of change in fibromyalgia. RMD Open. 2015;1(1):e000146.
54. Shor RE, Orne EC. Harvard Group Scale of Hypnotic Susceptibility. Palo Alto, California: Consulting Psychologists Press, INC; 1963.
55. Bennett RM, Friend R, Jones KD, Ward R, Han BK, Ross RL. The Revised Fibromyalgia Impact Questionnaire (FIQR): validation and psychometric properties. Arthritis Research & Therapy. 2009;11(4):R120-R.
56. Barry MJ, Fowler FJ, O'Leary MP, Cockett ATK. The American Urological Association Symptom Index for benign prostatic hyperplasia: The measurement committee of the American Urological Association. The Journal of Urology 1992;148(5):1549-57.
57. R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundatoin for Statistical Computing; 2010.