Official Title: Bronx Mindfulness-Based Cognitive Therapy for Migraine Trial

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1) Objective

The current phase 2b study aimed to evaluate the efficacy of Mindfulness-Based Cognitive Therapy for Migraine (MBCT-M) to reduce migraine-related disability in people with migraine compared to wait list/treatment as usual (WL/TAU).

2) Study Design

This is a randomized clinical trial (RCT) testing an 8-week, MBCT-M intervention (involving 8 weekly, 75-90 minute individual sessions) vs waitlist/treatment as usual (WL/TAU) in people with migraine (N=60), with follow-up assessments at 1 and 6 months post-treatment (the latter will be for the treatment group only). This is a Phase IIb trial (ORBIT Model).

3) Study Population

We recruited 60 participants, and randomized 31 participants to MBCT-M and 29 to WL/TAU. Recruitment and randomization was stratified by episodic migraine (< 15 headache days/month) and chronic migraine (>=15 headache days/month). Inclusion criteria were a) currently meeting International Classification of Headache Disorders (ICHD)-3 beta headache diagnosis for migraine using a semi-structured clinical interview and the validated American Migraine Study/American Migraine Prevalence and Prevention Study migraine diagnostic screener[36], b) self-reported and prospective diary-confirmed ≥ 6 headache days per month, c) aged 18-65, d) ability to read English, and e) capacity to consent. Exclusion criteria were a) continuous headache over the course of 30 days, b) initiation of a preventative migraine treatment within four weeks of the baseline assessment or a plan to initiate preventive migraine treatment during the duration of the study, c) severe psychiatric illness that would interfere with participation in the treatment such as active suicidality, active psychosis, or failing a cognitive screen, or d) inability to adhere to headache diary during baseline period (recorded fewer than 26/30 days).

4) Participant Recruitment

Participants were recruited from neurology office referrals and local and online advertisements in the broader New York City area including New York, New Jersey and Connecticut. Participants were provided with the MBCT web page information, our team email and office phone number. All potential subjects were screened by study staff online or via a telephone call prior to the intake appointment.

5) Informed Consent

After screening, participants attended a baseline assessment visit where they will again be screened for eligibility. If eligible, participants were given the opportunity to provide written informed consent.

5) Procedure:

Those who consented to participation in this study completed a baseline assessment with a study coordinator. At the baseline assessment, participants completed a self-report questionnaire for demographic information and symptom severity, and completed baseline psychosocial surveys using the REDCap electronic data capture system, a secure data capture program available through Albert Einstein College of Medicine. Participants were given access to the REDCap Headache Diary Application for the duration of the four-week baseline assessment. If the participant did not have an iPhone or iPod touch, an iPod Touch was provided. The study coordinator provided education and orientation to the use of the headache diary application as well as the reminder system that will guide participants to optimal completion. At the conclusion of the 4-week baseline assessment period, all participants will complete psychosocial measures again via REDcap through an

email reminder.

Study participants received up to $70 for participating in the study.

Participants who continue to meet study inclusion/exclusion criteria will be randomized to either the MBCT-M or WL/TAU group. We will use a randomization procedure stratified by episodic vs. chronic migraine based on headache days/month recorded in the daily headache diary. A statistician otherwise unrelated to the study useda computerized random number generator to randomize participants in random blocks of 2, 4, and 6 participants stratified by headache days/month (cut off score of 15).

During the 8-week treatment phase, participants randomized to the MBCT-M intervention group attended 8 weekly individual 75-90 minute sessions using a treatment protocol adapted from the MBCT for Chronic Headache Pain manual by Melissa Day, Ph.D., and Beverly Thorn, Ph.D. Each session included education, cognitive exercises designed to demonstrate how to think mindfully, and in-vivo mindfulness meditation practice designed to help participants systematically gain mindfulness skills throughout the course of treatment. Participants were given "homework," including formal mindfulness meditation and informal mindful awareness exercises, labeling thoughts, identifying warning signs for stress and migraine, and planning nourishing activities, in between sessions. Homework was assigned each week, and participants were expected to develop a daily formal mindfulness practice (body scan meditation, seated meditation, breathing meditation). Participants were provided with a course manual, reading materials, and audio recordings to facilitate meditation practice. The weekly sessions were be conducted by a clinical psychology student who had completed his or her master's level training in the clinical psychology, health emphasis Ph.D. program at Ferkauf Graduate School of Psychology. All therapists completed training conducted by Dr. Melissa Day, who developed the MBCT for Chronic Headache Pain manualized treatment. The doctoral level students received clinical supervision from licensed and credentialed clinical psychologists. During the eight weeks of intervention, participants randomized to the MBCT intervention group continued to complete daily headache diary and record daily formal mindfulness practice for eight weeks. All sessions were audio-recorded and coded for treatment fidelity by two independent raters. Participants randomized to the WL/TAU group did not take the headache diary for the 8 week treatment period.

At the conclusion of the 8-week treatment period, all participants (in both the MBCT-M group and the WL/TAU group) completed headache diaries for 4 weeks. At the conclusion of the four weeks, participants completed one final set of psychosocial measures through the REDCap electronic data capture system. At this point, participants in the WL/TAU group were offered participation in MBCT-M.

Participants randomized to the MBCT group were asked to complete the psychosocial measures 6 months after completion of MBCT through the REDCap electronic data capture system.

Measures

Measures include the following:

Baseline Survey

We will ask demographics questions pertaining to age, gender, race and ethnicity, as well as validated questions about headache symptoms (AMPP diagnostic module). The latter will help investigators determine an International Classification of Headache Disorders – 3 beta headache diagnosis for each participant.

Headache Diary

Via the iPod Touch/Diary REDCap application, a daily headache diary will assess:

- Headache Day: Number of days on which headache was reported in a month.

- Headache Severity: Day-level headache severity with response options including 0 (None), 1 (Mild), 2 (Moderate), 3 (Severe). Average headache severity will be aggregated by month.
- Migraine Disability Index: (MIDI) a four-item scale that assesses disability related to four domains (Family and Home, Recreation, Social Activity, Job/Occupation). For each domain, an 11-point Likert scale allows for possible ratings of 0 (not at all) to 10 (totally).The four ratings are averaged; the final score is in the 0-10 range with higher scores indicating higher disability. Average day-level migraine disability (MIDI) score will be aggregated by month.

Psychosocial Surveys

- The Migraine Disability Assessment (MIDAS; primary outcome) is a 5-item, self-report instrument measuring disruption experienced due to migraine. Items target role functioning and ask about lost days of house-work, job-work, and non-work activities. Each item is an open question, allowing entry of number of days lost over 90 days. Total scores range from 0-450, and are categorized as <21 (Low Disability) and >=21 (Severe Disability).
- The Headache-Related Disability Index (HDI; primary outcome) is a 25-item, self-report questionnaire of the emotional and functional impact of headache on daily activities. The items require a "yes," "no," or "sometimes," response to assess participants' perceived headache-related disability. Total scores range from 0-100; higher scores indicate higher disability.
- The Pain Catastrophizing Scale (PCS) is a 13-item self-report measure that conveys a participant's level of pain-related, catastrophic thinking during painful experiences. The measure has three subscales: Rumination (4 items), Magnification (3 items) and Helplessness (6 items). Ratings are made on a 5-point scale from 0 (not at all) to 4 (all the time). Total scores range from 0 to 52; higher scores indicate higher catastrophizing.
- The Chronic Pain Acceptance Questionnaire (CPAQ) is a 20-item, self-report measure of pain-related acceptance, developed among chronic pain populations. Each item is rated on a Likert scale ranging from 0-7, with total scores ranging from 0-140, with higher scores indicating higher levels of acceptance.
- The Headache Specific Locus of Control (HSLC) is a 33-item measure designed to assess the extent to which individuals with recurrent headaches expect that the occurrence, worsening, and improvement of their headaches are influenced primarily by their own behavior (Internal), by chance or fate (Chance), or by the actions of medical professionals (Medical Professionals). Items are coded on a 5-point Likert-type scale ranging from 1 (strongly agree) to 5 (strongly disagree); total HSLC ranges from 33-165, with higher scores indicating more external locus of control.
- The Five Facet Mindfulness Questionnaire (FFMQ) is a 39-item self-report instrument containing five subscales: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. Each item has a 5-point response scale ranging from 1 (never or very rarely true) to 5 (very often or always true). Total scores range from 39-195 with higher scores indicating higher levels of mindfulness.
- The Headache Management Self-efficacy Scale (HMSE) is 25-item self report scale designed to capture the confidence a patient believes they have in their own abilities to prevent headache episodes and manage their pain. Each item is rated on a Likert scale ranging from 1-7, ranging from 1 (strong disagree) to 7 (strongly agree). Total scores range from 25 to 175 with higher scores indicating a higher degree of self-efficacy.
- The NIH PROMIS depression Short Form is an 8-item self-report measure developed by the National Institutes of Health that assesses emotional distress "in the past 7 days," focusing on negative mood and negative self-views. Ratings are made on a 6-point scale, from 1 (Never) to 5 (Always). Scores are calibrated to a T score metric (M = 50, SD = 10) normed to U.S. population demographic means. Higher scores represent more severe depressive symptomology.
- The NIH PROMIS Anxiety Short Form is an 8-item self-report measure developed by the National Institutes of Health that assesses emotional distress "in the past 7 days," focusing on fear, worry and hyper-arousal. Ratings are made on a 6-point scale, from 1 (Never) to 5 (Always).

Scores are calibrated to a T score metric (M = 50, SD = 10) normed to U.S. population demographic means. Higher scores represent more sever anxiety symptoms.

6) Data Analysis

Distributions of all study variables were evaluated for normality, skewness and kurtosis. Day-level imputation was used to impute missing diary data points (15.5%) for headache diary measures. Variables at baseline were described using mean and standard deviation for normally distributed variables, and number and percent for nominal variables. Differences between treatment groups for primary and secondary outcomes at baseline were evaluated using t-tests and chi-squares.

Intent-to-treat analysis used linear (continuous variables) and logistic (dichotomous variables) mixed models for repeated measures to estimate missing values and evaluate changes in outcomes. For survey variables, time was a 4-level variable (Month 0, 1, 2, and 4); for diary data, time was a two-level variable (baseline monitoring period vs. post-treatment evaluation period). Fixed effects were group, time, and their interaction. A significant interaction indicated the slope of the MBCT-M group differed from the slope of the WL/TAU group. Random effects were intercept and time. Akaike's information criterion indicated a first-order autoregressive covariance structure was appropriate for modeling month.