Published in final edited form as:

Headache. 2018 June ; 58(6): 859–872. doi:10.1111/head.13325.

Acceptance, Psychiatric Symptoms and Migraine Disability: An Observational Study in a Headache Center

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Abstract

Objective—To evaluate relationships between psychiatric symptoms, acceptance, and migraine-related disability in a sample of people with migraine presenting at a tertiary care headache center.

Background—Migraine is a chronic disease that can be severely disabling. Despite a strong theoretical basis and evidence in other pain conditions, little is known about relationships between acceptance, psychiatric symptoms, and migraine-related disability.

Methods—Ninety patients with physician-diagnosed migraine completed surveys assessing demographics, headache symptoms, severe migraine-related disability (Migraine Disability Assessment Scale total score dichotomized at 21), depression (Patient Health Questionnaire-9) and anxiety symptoms (Generalized Anxiety Disorder-7), and acceptance (Chronic Pain Acceptance Questionnaire; subscales: Pain Willingness and Activity Engagement).

Results—Participants (77.8% White, Non-Hispanic; 85.6% women; and 50.0% with a graduate level education) reported an average headache pain intensity of 6.7/10 (SD = 2.0). One-third (36.0%) reported chronic migraine, and half (51.5%) reported severe migraine-related disability. Lower acceptance was associated with severe migraine-related disability, $t(54) = 4.13, p < .001$. Higher activity engagement was associated with lower average headache pain intensity ($r = -.30, p = .011$). Higher acceptance was associated with lower levels of depression ($r = -.48, p < .001$) and anxiety symptoms ($r = -.37, p = .003$). Pain willingness and activity engagement serially mediated relationships between depression symptoms and severe migraine-related disability (indirect effect = 0.05, 95% CI = 0.01, 0.15), and between anxiety symptoms and severe migraine-related disability (indirect effect = 0.12, 95% CI = 0.02, 0.31).

Conclusion—Results provided preliminary support for a theoretical pathway by which psychiatric symptoms may influence migraine-related disability, in part, through their relationships with pain willingness and activity engagement.

Keywords

Migraine; Acceptance; Disability; Anxiety; Depression

Introduction

Migraine is a chronic neurologic disease with episodic manifestations affecting 12–17% of the adult population annually^{1,2} and is a leading cause of disability worldwide.³ The impact of migraine on daily functioning stems not only from pain and other associated symptoms but also from the experience of stigma about inability to fulfill role obligations,⁴ social withdrawal,⁵ and comorbid psychiatric conditions.⁶ Major depression and anxiety disorders are disproportionately prevalent in migraine,^{7,8} and the prevalence and impact of these comorbid psychiatric conditions increase with headache frequency.⁹ Further, higher levels of depressive and anxious symptoms have been associated with increased migraine-related disability among people with migraine.^{7,10}

Numerous psychological theories suggest that patterns of thinking and responding can influence migraine-related disability. A growing number of studies suggest that one's maladaptive responses to pain (e.g., fear of pain, pain catastrophizing) are as or more predictive of functional impairment and disability than pain symptomatology.^{11–14} More recently, studies have begun to evaluate potentially adaptive behavioral responses to pain. Acceptance is posited to be an adaptive response to pain, and denotes a willingness to nonjudgmentally experience internal (private) events, even if they are aversive (e.g., fearful thoughts, pain sensations, negative emotions).¹⁵ Acceptance of pain thus involves a willingness to experience or endure pain sensations (pain willingness) and remain engaged in activities despite pain (activity engagement), particularly activities consistent with broader life goals and values.¹⁶

The extant research suggests that pain-related acceptance plays a significant role in migraine-related disability. A recent study of 103 treatment-seeking people with migraine found that both components of pain acceptance (pain willingness and activity engagement) were more strongly associated with disability than was headache frequency or intensity.¹⁷ A recent study of 126 women seeking treatment for weight loss and migraine found that higher pain willingness, but not activity engagement, was associated with lower headache-related disability when adjusting for headache frequency and intensity,¹⁸ suggesting that evaluation of the separate components of acceptance may be relevant in migraine. Two small trials of a behavioral treatment that seeks to cultivate pain acceptance (Acceptance and Commitment Therapy) demonstrated larger effects in reduction of headache-related disability than in reductions of headache intensity or frequency.^{20,21}

The theoretical framework that guides research and clinical work on acceptance suggests that lack of acceptance, or experiential avoidance, contributes to the development and maintenance of anxiety and depression by reinforcing rigid patterns of thinking and behavior, unlinked from the context in which the behavior occurs²². Empirically, higher acceptance has been associated with less severe depression and anxiety symptomatology,²³ and meta-analyses of acceptance-based interventions suggest that increasing acceptance

facilitates reductions in depression and anxiety.^{24,25} A recent study of 93 people with migraine and major depressive disorder found that lower pain-related acceptance was associated with more severe depression symptoms. Pain-related acceptance also contributed unique variance in headache-related disability beyond depressive symptoms alone.²⁶ A second recent study of 224 people recruited online with self-reported migraine found that higher acceptance was associated with lower headache impact and depression symptoms, even when controlling for demographics and other theoretically relevant psychological factors¹⁹. Given the theoretical and empirical links between psychiatric symptoms and acceptance, it is possible observed associations between psychiatric symptoms and migraine-related disability in migraine occur, in part, through acceptance. Specifically, higher levels of depressive and anxious symptoms have demonstrated associations with lower levels of pain willingness and activity engagement, and these relationships may lead to higher levels of migraine-related disability in people with migraine. No study to date has assessed this theory-based pathway in people with migraine.

The current study aims to evaluate these theoretically relevant relationships between psychiatric symptoms, headache-related acceptance (pain willingness and activity engagement), and both migraine-related disability (primary outcome) and migraine symptom variables (chronic migraine vs. episodic migraine and average headache pain intensity; secondary outcomes) in a naturalistic sample of people with migraine presenting at a tertiary care headache center. We hypothesized that higher headache-related acceptance would be associated with lower levels of psychiatric symptoms, migraine-related disability, and migraine symptom variables. Consistent with the theoretical conceptualization that pain willingness is necessary to facilitate activity engagement,^{16,27} we also hypothesized that headache-related acceptance would serially mediate the relationship between psychiatric symptoms and migraine-related disability, such that more severe psychiatric symptom levels would be associated with lower pain willingness, which would be associated with lower activity engagement, which would be associated with higher levels of migraine-related disability. Understanding the relationships among psychiatric symptoms, cognitive and behavioral responses to pain, and migraine-related disability in the context of migraine provides evidence necessary to develop interventions aimed at reducing such disability among people with migraine and comorbid mood and/or anxiety disorders.

Methods

Participants

These planned secondary analyses are part of a survey study designed to evaluate individual differences in psychiatric symptoms, avoidance, and acceptance, and their association with migraine symptoms, characteristics and headache-related disability in people with migraine presenting to a tertiary care outpatient clinic for routine care.¹⁴ Consecutive patients were recruited from the waiting room of a headache center in the Bronx, NY. Inclusion criteria were: 1) current physician diagnosis of migraine, 2) currently met criteria for migraine according to the International Classification of Headache Disorders (ICHD-3 beta)²⁸ using the American Migraine Study (AMS/American Migraine Prevalence and Prevention (AMPP) study diagnostic module),^{29,30} 3) aged 18 and over, 4) ability to read English, and

5) capacity to consent. A priori power analysis for the primary study [examining the bivariate associations between psychiatric variables and migraine symptoms and disability using linear and/or logistic regression, with an assumptions of $r = .30$ or $OR = 2.0$ based on previous literature and an alpha of .05] indicated a required minimum sample of $n = 80$ for a power of .80 across analyses. We planned to recruit 110 participants to ensure we reached 80 eligible and complete surveys.

Procedure

From May – August, 2014, psychology graduate students approached patients in the waiting room of a tertiary care headache center located within an urban hospital and screened for inclusion criteria. Patients who reported meeting inclusion criteria gave informed consent and completed a packet of surveys assessing demographics, headache and migraine symptoms and associated disability, psychiatric symptoms, and psychosocial measures relevant to headache disorders including acceptance. The majority of participants completed the survey packet while in the waiting room; participants who did not complete the survey packets prior to leaving the headache center mailed the completed surveys back to study staff using a self-addressed stamped envelope ($n = 8$). Participants received a \$10 gift card to either Amazon or Target in exchange for their voluntary participation. The study protocol was approved by the Albert Einstein College of Medicine Institutional Review Board (#2013-2859), and was supported through institutional funds awarded to the first author.

Study staff consented a total of 110 headache center patients for participation in this study; 95 of these participants returned the surveys. Five participants who completed surveys did not have a current physician diagnosis of migraine recorded in their electronic health record and were therefore excluded from the analyses. Therefore, 90 participants met inclusion criteria and were included in the study.

Measures

Demographics—Participants reported their age (continuous), gender (male or female), race (White, Black/African American, Native American, Asian, Pacific Islander, Other), ethnicity (Hispanic or Non-Hispanic), marital status (single, married, separated/divorced, widowed, live with a domestic partner), and highest level of education completed (8 grades or less, some high school, high school graduate or GED, some college or technical school, college graduate, graduate degree). For bivariate relationships, race/ethnicity (White, Non-Hispanic vs. Other), marital status (married/live with a domestic partner vs. single/separated/divorced/widowed), and education (graduate degree vs. all else) were evaluated dichotomously.

Migraine Diagnosis—Physician diagnosis of migraine was determined through chart review using electronic health records.

The validated American Migraine Study/American Migraine Prevalence and Prevention Study diagnostic module was used to assess ICHD-2³¹ current criteria for migraine via patient self-endorsement of symptoms. Items asked about symptoms in relation to headache and include the ICHD diagnostic criteria including unilaterality of headache pain (e.g., “The

pain is worse on just one side”) and associated symptoms (e.g., “You feel nauseated or sick to your stomach or vomit”). A 4-point Likert type response option scale indicates frequency of symptom experience in relation to headache (“Never” to “Half the Time or More”). This diagnostic module has demonstrated a sensitivity of 100% and a specificity of 82% for migraine²⁹ using ICHD-2 criteria, which were in use at the time. No changes to the migraine criteria were made between ICHD-2 and ICHD-3²⁸ criteria versions.

Migraine Disability Assessment (MIDAS)—The Migraine Disability Assessment³² is a 5-item self-report measure designed to measure disability due to migraine. Items assess the number of days of house-related work, job-related work, and non-work activities lost (absenteeism) or reduced (presenteeism) due to migraine over the last three months. Two additional questions measure headache frequency (headache days per month) and average headache pain intensity: the first assesses the number headache days over the past three months (divided by 3 to obtain the number of headache days in the past month) and the second assesses the pain intensity of these headaches on a scale from 0–10. Several studies show the MIDAS to have good internal consistency ($\alpha = 0.76$), reliability and validity and suggest that it is useful for improving healthcare in clinical settings.³³ In our sample, the MIDAS demonstrated excellent internal consistency ($\alpha = 0.94$). Because MIDAS scores reflect frequency counts that are often positively skewed, we utilized clinical cut-offs established during scale development indicating severe migraine-related disability (MIDAS Score ≥ 21)³² and analyzed data dichotomously.

Chronic Pain Acceptance Questionnaire (CPAQ)—The CPAQ³⁴ is a 20-item self-report measure of pain-related acceptance that was developed and validated in chronic pain populations. Each item is rated on a Likert scale ranging from 0 (“Never True”) to 6 (“Always True”); higher scores indicate higher pain-related acceptance. The scale has demonstrated validity in chronic pain samples.³⁴ Initial cognitive interviewing with patients revealed that using “pain” as the prompts for scale items lead to confusion. We therefore substituted the word “pain” with the word “headache,” which participants reported understanding more clearly. The measure contains two subscales, Activity Engagement (“I lead a full life even though I have headaches”) and Pain Willingness (“Before I can make any serious plans, I have to get some control over my headaches”). Principal Component Analysis using Horn’s Parallel Analysis and varimax rotation identified two components which accounted for 43.8% of the variance in scores and broadly corresponded with existing subscales, Activity Engagement (eigenvalue = 6.52) and Pain Willingness (eigenvalue = 2.23), although several Pain Willingness items loaded more strongly on the Activity Engagement component in this analysis (“My worries and fears about what headache will do to me are true”, reverse coded, Activity Engagement loading = .61, Pain Willingness loading = $-.22$; “I have to struggle to do things when I have headaches,” reverse coded, Activity Engagement loading = .64, Pain Willingness loading = .08). Internal consistency in our sample was excellent for both the total scale ($\alpha = 0.89$) and Activity Engagement subscale ($\alpha = 0.87$) and adequate for the Pain Willingness subscale ($\alpha = .75$).

Patient Health Questionnaire (PHQ-9)—The PHQ-9³⁵ is a 9-item self-report measure designed to capture symptoms of depression to assess criteria as defined in the Diagnostic

and Statistical Manual of Mental Disorders, Fourth Edition.³⁶ These criteria have not changed substantively in the updated fifth edition.³⁵ The scale was developed with adult patients of primary care clinics. Items are rated from 0 (“Not at all”) to 3 (“Nearly every day”), with total scores ranging from 0 to 27 and higher scores indicating greater severity of depression symptoms. Clinical cut-offs established during scale development are 5 (“mild depression”), 10 (“moderate depression”), 15 (“moderately severe depression”), and 20 (“severe depression”).³⁵ In development studies, the PHQ-9 demonstrated excellent internal consistency ($\alpha = 0.86\text{--}0.89$) and test-retest reliability ($r = 0.84$), as well as good criterion and construct validity.³⁵ In our sample, the scale demonstrated good internal consistency ($\alpha = 0.88$) and factor structure comparable to that reported in the literature.

Generalized Anxiety Disorder (GAD-7)—The GAD-7³⁸ is a 7-item self-report measure of Generalized Anxiety Disorder criteria as defined in the DSM-IV. These criteria also have not changed substantively in the updated fifth edition (DSM-5).³⁷ The GAD-7 has also demonstrated validity as a screener for other anxiety disorders, including panic disorder, social phobia, and PTSD.³⁹ The scale was developed with adult patients of primary care clinics. Items are rated from 0 (“Not at all”) to 3 (“Nearly every day”), with total scores ranging from 0 to 21 and higher scores indicating greater severity of anxiety symptoms. Clinical cut-offs established during scale development are 5 (“mild anxiety”), 10 (“moderate anxiety”), and 15 (“severe anxiety”).³⁸ In psychometric studies, the GAD-7 demonstrated good internal consistency ($\alpha = 0.92$) and test-retest reliability ($r = 0.83$), as well as good criterion, construct, factorial, and procedural validity.³⁸ In our sample, the scale demonstrated good internal consistency ($\alpha = 0.91$) and factor structure comparable to that reported in the literature.³⁹

Analysis

Descriptive statistics and distributions were evaluated for all study variables. Means and standard deviations, medians and interquartile ranges, or Ns and percentages are reported for all variables. Bivariate relationships among CPAQ total and subscale scores and demographics, migraine variables [migraine diagnosis and headache day frequency (Chronic Migraine vs. Episodic Migraine), average headache pain intensity, and severe migraine-related disability (MIDAS 21)] and psychosocial variables (PHQ-9, GAD-7, and HSLC subscales, all evaluated continuously) were evaluated using t-tests for continuous and categorical variables, Pearson correlations for two normally-distributed variables, and Spearman correlations when one variable was skewed. For bivariate analyses among CPAQ scores and other study variables, a Bonferroni-Holm correction procedure was applied to adjust for multiple comparisons. For bivariate analyses, sensitivity analyses using multiple imputation assessed the extent to which missing data influenced results. Multiple imputation estimates missing data points using all available data as predictors of each missing data point in a linear model. These sensitivity analyses were performed for each scale at the item-level, with models including all scale items, gender, and age.

Conditional process analysis (PROCESS)⁴⁰ using a series of regressions evaluated the hypothesis that the CPAQ subscales mediated observed relationships between psychiatric symptoms and severe migraine-related disability (MIDAS 21). Existing theory suggested a

serial mediation was most appropriate: psychiatric symptoms decrease pain willingness, which in turn decreases activity engagement, and ultimately increases migraine-related disability (Figure 1). Conditional process analysis directly tested these mediation hypotheses by constructing a series of regression models. In the first, Pain Willingness served as the outcome variable, and the psychiatric symptom as the predictor variable. In the second, Activity Engagement served as the outcome variable, and with both the psychiatric symptom and Pain Willingness as predictor variables. In the third, severe migraine-related disability (MIDAS ≥ 21) served as the outcome, with the psychiatric symptom, Pain Willingness, and Activity Engagement serving as predictors in the model. Finally, a bootstrapping procedure estimates 10,000 random samples of the indirect (serial mediation) effect, a parameter which combines the psychiatric symptom parameter attained from the first model, the Pain Willingness parameter obtained from the second model, and the Activity Engagement parameter obtained from the third model. If the 95% confidence interval of the indirect effect parameter does not include zero, the serial mediation is significant. As part of serial mediation, we also evaluated both Pain Willingness and Activity Engagement simple mediational pathways (Figure 1). Missing data for mediation analyses was addressed using complete case analysis, since the regression procedures underlying conditional process analysis rely on complete cases.

SPSS version 25 was used for all analyses, with the PROCESS macro for conditional process analysis and the RAWPAR macro for Horn's Parallel Analysis. Alpha was set at .05, two-tailed, for all analyses.

Results

Descriptive Statistics

All participants had been diagnosed with migraine by a neurologist. Participants ($n = 90$) were predominantly White, Non-Hispanic (77.8%) married (60.7%) women (85.6%) with graduate level education (50.0%) (Table 1). On average, participants reported 13.0 ($SD = 12.9$; $n = 89$) headache days per 30 days and an average headache pain intensity of 6.7 ($SD = 2.0$; $n = 89$) on a 0 to 10 scale, indicating moderate to severe headache pain intensity. One-third of participants (32/89; 36.0%) reported 15 or more headache days/month, indicating chronic migraine. Sixty-eight participants completed the full MIDAS questionnaire using discreet integers (e.g., participants who answered any question with a series of ranges or detailed descriptions that did not include a clear integer, or who declined to answer a question, were excluded). The median MIDAS total score was 22.0 (IQR = 5.0, 47.0), indicating severe migraine-related disability. Approximately half (35/68; 51.5%) of participants reported severe migraine-related disability (MIDAS total score ≥ 21).

Sixty-nine participants completed all CPAQ items, 74 completed all Pain Willingness items, and 79 completed all Activity Engagement items. The average CPAQ total score was 56.1 (18.4). The average Pain Willingness subscale score was 23.6 ($SD = 8.5$). The average Activity Engagement subscale score was 32.6 ($SD = 12.6$). Both the Activity Engagement ($r = .92$, $p > .001$) and Pain Willingness ($r = .83$, $p < .001$) subscales were highly correlated with higher CPAQ total score. The Activity Engagement and Pain Willingness CPAQ subscales were more modestly correlated with each other, $r = .56$, $p < .001$. Both CPAQ

Total ($M_s = 48.1$ vs. 61.0 , $p = .013$) and CPAQ Activity Engagement ($M_s = 25.9$ vs. 36.1 , $p = .004$) were lower among people who identified as White, Non-Hispanic compared to all other racial and ethnic groups. No other demographic characteristic was associated with the CPAQ total [age $r = .04$, $p = .772$; education $t(66) = 1.08$, $p = .287$; marital status $t(66) = -1.21$, $p = .232$], Pain Willingness [age $r = .02$, $p = .882$; education $t(71) = 0.48$, $p = .630$; marital status $t(71) = -0.14$, $p = .891$], or Activity Engagement [age $r = .05$, $p = .692$; education $t(76) = 0.19$, $p = .851$; marital status $t(76) = -1.37$, $p = .176$]; gender was not evaluated, as all cell sizes were <10 for men.

Bivariate Relationships between CPAQ and Study Variables

Lower CPAQ total [$t(54) = 4.13$, $p < .001$], Pain Willingness [$t(56) = 2.99$, $p = .004$] and Activity Engagement [$t(61) = 4.12$, $p < .001$] were associated with severe migraine-related disability (MIDAS Score ≥ 21). Higher Activity Engagement was associated with lower average headache pain intensity ($r = -.30$, $p = .011$). No CPAQ score was associated with migraine diagnosis [CPAQ Total $t(64) = 1.56$, $p = .124$; Pain Willingness $t(68) = 0.67$, $p = .508$; Activity Engagement $t(73) = 1.40$, $p = .167$].

On average, participants reported mild levels of depression symptoms ($M = 5.5$, $SD = 4.9$; $n = 85$) and minimal levels of anxiety symptoms ($M = 3.7$, $SD = 4.0$; $n = 83$). Higher CPAQ total and subscale scores were associated with lower psychiatric symptoms across all measures. Higher CPAQ total scores and CPAQ Pain Willingness subscale scores were associated with lower depression symptoms (CPAQ Total $r = -.48$, $p < .001$; CPAQ Pain Willingness $r = -.50$, $p < .001$) and lower anxiety symptoms (CPAQ Total $r = -.35$, $p = .003$; CPAQ Activity Engagement $r = -.31$, $p = .008$). In contrast, higher CPAQ Activity Engagement Subscale scores demonstrated a medium correlation with both lower depression and anxiety symptoms (GAD-7 $r = -.31$, $p = .008$; PHQ-9 $r = -.31$, $p = .005$).

Sensitivity analyses revealed comparable findings when comparing results obtained using observed data (presented above) and those obtained using all multiple imputation datasets constructed.

Mediation Analyses

Conditional process analysis with depression (PHQ-9) serving as the predictor variable supported the serial mediation hypothesis (serial mediation indirect effect = 0.05 , 95% CI = $0.01, 0.15$) and the activity engagement simple mediation hypothesis (indirect effect = 0.05 , 95% CI = $0.01, 0.14$) (Figure 2a). Regarding serial mediation, higher depression symptoms were associated with lower pain willingness ($B = -0.76$, $p < .001$); higher pain willingness was associated with higher activity engagement ($B = 0.77$, $p < .001$); and higher activity engagement was associated with lower odds of severe migraine-related disability ($B = -0.09$, $p = .027$). Regarding simple mediation, higher depression symptoms were associated with lower activity engagement ($B = -0.59$, $p = .022$); and higher activity engagement was then associated with lower odds of severe migraine-related disability (-0.09 , $p = .027$).

Conditional process analysis with anxiety (GAD-7) serving as the predictor variable supported the serial mediation hypothesis (serial mediation indirect effect = 0.12 , 95% CI = $0.02, 0.31$) (Figure 2b). Higher anxiety symptoms were associated with lower pain

willingness ($B = -1.17, p < .001$); higher pain willingness was associated with higher activity engagement ($B = 0.91, p < .001$); and higher activity engagement was associated with lower odds of severe migraine-related disability ($B = -0.11, p = .009$).

Discussion

This study found that lower headache-related acceptance was associated with severe migraine-related disability among a sample of people with migraine presenting at a tertiary care headache center. Higher activity engagement, one component of headache-related acceptance, was associated with lower headache pain severity. Further, both components of headache-related acceptance (pain willingness and activity engagement) were associated with psychiatric symptoms, such that lower levels of pain willingness and activity engagement were associated with higher levels of depressive and anxiety symptoms. Finally, this study provided preliminary support for a theoretical pathway by which psychiatric symptoms influence migraine-related disability, in part, through their relationships with pain willingness and activity engagement. These results add to the body of literature supporting the importance of adaptive cognitive responses to headache (such as acceptance) in understanding the lived experiences of people with migraine, and clarify the role headache-related acceptance may play in relationships between psychiatric symptoms and migraine-related disability.

Results indicate that lower headache-related acceptance is associated with severe migraine-related disability, consistent with previous findings in chronic pain broadly^{41–44} and migraine specifically.^{17,18,19} However, in contrast with previous research,¹⁸ results from this study suggest that both pain willingness *and* activity engagement play important roles in migraine-related disability. This is consistent with the behavioral link between activity engagement (remaining engaged in activities despite headache) and migraine-related disability as assessed in this study (number of days where role functioning was prevented or restricted due to migraine). Interestingly, Lillis and colleagues¹⁸ found that when adjusting for pain intensity and migraine frequency, pain willingness, but not activity engagement, was associated with lower headache-related disability in a sample of women with migraine and overweight/obesity seeking weight loss and migraine treatment. The authors did not report unadjusted analyses, therefore it is possible adjustments account for this discrepancy. Further, their study did not modify the CPAQ for use in a headache population, instead opting to keep the original prompt of “pain” in the items. People with migraine often experience other pain disorders,^{45,46} especially those who are receiving medical care,⁴⁷ and may respond to prompts about “pain” on psychosocial questionnaires considering these other pain conditions. This difference might have been particularly relevant in women with overweight/obesity seeking weight loss treatment, who can reasonably be expected to avoid activity engagement for reasons other than migraine, compared to a sample drawn from a general headache center population.

For anxiety, results supported the hypothesized pathway influencing migraine-related disability through acceptance. Results suggest that people with high anxiety are more likely to experience their current migraine symptoms as an unacceptable situation they need to control before they can make or keep commitments. This subsequently leads to a withdrawal

from daily activities and “living a normal life” (CPAQ item 6), which then restricts and prevents role functioning in occupational, educational, home, and social settings. This is consistent with psychological theories which emphasize of the importance of avoidance in perpetuating disability in painful conditions.^{16,27} These results provide insight into the psychological mechanisms that contribute to migraine-related disability and anxiety symptoms. These results also suggest that reduction of activity avoidance through specific acceptance-based approaches or through existing evidence-based cognitive and behavioral approaches, might be particularly useful in this subpopulation of people with migraine. Further, evaluating pain willingness and activity engagement as potential mechanisms of change across various behavioral migraine treatments could yield important information regarding shared mechanisms of treatment and help clinicians better utilize empirically-supported change mechanisms.

In this study, depression symptoms influenced migraine-related disability through both the hypothesized pathway described above (through both pain willingness and through activity engagement), and more directly through activity engagement. These results suggest higher depression symptoms lead to less engagement in daily activities (“getting on with the business of living”; CPAQ item 1), contributing to migraine-related disability. This result is consistent with both depression symptoms and treatments known to be effective for major depressive disorder. Anhedonia, or lack of enjoyment of previously pleasurable activities, is a hallmark symptom of major depressive disorder.³⁷ Compelling evidence from the psychology literature suggests behavioral activation alone (e.g., increasing engagement in pleasurable valued activities) is an effective treatment for depression.⁴⁸ It is likely that depression increases with activity avoidance as individuals become more isolated, lose contact with social support networks, and withdraw emotionally. In addition, physical activity including exercise is beneficial for migraine management, therefore the lack of physical activity may also negatively affect migraine on multiple levels. These results provide preliminary evidence that activity engagement could be a particularly salient treatment target to reduce migraine-related disability in people with migraine and high levels of depressive symptoms.

Limitations and future directions

The sample was overwhelmingly composed of highly educated White women. The race and gender distribution represent a limitation of this study as well as in the broad literature evaluating migraine. The very high average level of education is not reflective of the migraine population in most medical care settings or in the general population; further, migraine is more prevalent and impactful in lower socioeconomic strata, which may mean that our results underestimate the strengths of the observed relationships.⁴⁹ Further, the sample consisted of treatment-seeking people who were sufficiently distressed by their migraine to seek care at a headache center and may not generalize to people with migraine seeking treatment in general specialty settings or primary care settings, or those who are not seeking medical treatment. The effects of Berkson’s bias may also influence this sample in that they may have higher rates of depression, anxiety, higher headache-related disability and other measured variables than individuals in the general population who are not seeking care for migraine, which is estimated at more than half of people who meet criteria for

migraine.^{50,51} However, the relationships between these variables may still exist even if overall rates of depression and anxiety are lower in non-care seeking populations. Future work may measure and assess the relationships between these variables among people with migraine with less frequent attacks, who are treated in primary care, or those who do not seek medical treatment for migraine.

Our measures of headache symptoms, frequency, migraine-related disability, depression, anxiety and the psychosocial constructs assessed relied on self-report, which can be unreliable. However, migraine is a diagnosis which is only assessed by patient self-report of symptoms and this is a common practice in both clinical care and in observational studies. In addition, our assessment of these variables was conducted retrospectively, which can be more unreliable than daily diary monitoring. However, the MIDAS was previously validated against a daily diary and showed strong reliability.⁵² The measure of headache-related disability used in this study (MIDAS) only captures role prevention and restriction, but not other areas of life also impacted by migraine, including emotional functioning and mobility. Researchers should continue to develop patient-reported outcome measures of migraine-related disability that more comprehensively capture the migraine patient experience.^{53,54} We modified the CPAQ to ask patients about “headache” rather than “pain.” Although this is an alteration of a validated questionnaire, we believe that it more accurately captures the construct of acceptance in the context of the migraine patient population. Furthermore, our cognitive interviewing with migraine patients regarding item development, a method that has been successfully used for other psychosocial questionnaires developed in the pain literature,^{13,14} supports the utility of substituting “pain” with “headache”. Psychometric evaluation of the scale as used in this study suggested that the scale was broadly reliable and had a factor structure generally similar to the original CPAQ, although some Pain Willingness items loaded more heavily on the Activity Engagement subscale. Given evidence for the importance of acceptance in migraine and headache disorders, future research should consider developing a headache-specific acceptance scale, which would propel forward research and intervention development in this area.

We did not evaluate the mediations separately for people with chronic vs. episodic migraine. There are theoretical reasons to think that pain willingness may be more relevant and useful for people experiencing near constant symptoms that may be treatment refractory (such as chronic migraine), whereas pain willingness may be less relevant and useful for people experiencing episodes of symptoms that can be effectively managed if identified and addressed quickly (such as episodic migraine). Our sample size was not large enough to allow us to evaluate the mediations by subgroup. Future studies should consider collecting larger samples or combining samples to ask these clinically and theoretically relevant questions.

Clinical Implications

This study indicates that headache-related acceptance was associated with lower pain intensity and migraine-related disability, and that components of acceptance (pain willingness and activity engagement) mediate well-established relationships between psychiatric symptoms and headache disability. Fostering headache-related acceptance may

thus be particularly important for people with migraine with high levels of depression and anxiety symptoms. Incorporating therapeutic methods such as Acceptance and Commitment Therapy⁵⁵ to enhance pain willingness (willingness to experience or endure migraine) and activity engagement (remaining engaged in valued activities despite migraine), such as through progressive exposure to headache stimuli or behavioral activation,^{56,57} could be useful additions to existing well-established biobehavioral interventions including cognitive-behavioral treatments, biofeedback and relaxation training to reduce migraine-related disability, particularly among patients with depression and/or anxiety symptoms.⁵⁸

Acknowledgments

The authors would like to acknowledge the contributions of Jaclyn Klepper, MA, Alexandra Singer, MA, Amy Grinberg, MA, and Annalisa Scuiillo, MA, for their assistance with this study, and all of the staff and providers at the Montefiore Headache Center.

Elizabeth Seng, Ph.D. in the past 12 months, has received funding from the National Institute of Neurological Diseases and Stroke (K23 NS096101 PI:Seng) and served as a consultant for GlaxoSmithKline. Todd Smitherman, Ph.D., in the past 12 months, has served as a consultant for Alder. Dawn C. Buse, Ph.D. in the past 12 months, has received grant support and honoraria from Allergan, Amgen, Avanir, Biohaven, Eli Lilly and Promeius. She is on the editorial board of *Current Pain and Headache Reports*, *the Journal of Headache and Pain*, *Pain Medicine News*, and *Pain Pathways* magazine.

Financial Support: This work was supported by institutional funds from Yeshiva University and the National Institute of Neurological Diseases and Stroke (K23 NS096107 PI:Seng).

Abbreviations

ICHD-3	International Classification of Headache Disorders, 3rd Edition
AMS	American Migraine Study
AMPP	American Migraine Prevalence and Prevention study
ICHD-2	International Classification of Headache Disorders, 2nd Edition
MIDAS	Migraine Disability Assessment Scale
CPAQ	Chronic Pain Acceptance Questionnaire
PHQ-9	Patient Health Questionnaire
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
GAD-7	Generalized Anxiety Disorder brief measure
PROCESS	conditional process analysis

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Figure 1.

Figure 2.

Table 1**Patient Characteristics**

Patient Characteristics (n)	M (SD) or N (%)
Demographics	
Age (<i>n</i> = 90)	45.0 (12.4)
Gender (<i>n</i> = 90)	
Male	13 (14.4%)
Female	77 (85.6%)
Race/Ethnicity (<i>n</i> = 90)	
White, Non-Hispanic	70 (77.8%)
Hispanic	10 (11.1%)
Black, Asian, Other, Non-Hispanic	10 (11.1%)
Education (<i>n</i> = 90)	
High school or less	9 (10.0%)
Some college/technical school	13 (14.6%)
College graduate	22 (24.4%)
Graduate degree	45 (50.0%)
Marital Status (<i>n</i> = 90)	
Single	28 (31.5%)
Married/living with domestic partner	54 (60.7%)
Separated/divorced/widowed	7 (7.8%)
Headache Characteristics	
Migraine Diagnosis (<i>n</i> = 89)	
<i>Chronic Migraine (≥ 15 days/month)</i>	32 (36.0%)
<i>Episodic Migraine (<15 days/month)</i>	57 (64.0%)
Average Headache Pain Intensity (0–10) (<i>n</i> = 89)	6.7 (2.0)
MIDAS (<i>n</i> = 68)	
<i>Severe Disability (≥ 21)</i>	35 (51.5%)
<i>Mild-Moderate Disability (<21)</i>	33 (48.5%)

MIDAS = Migraine Disability Assessment Score

Table 2

Bivariate Relationships between CPAQ and Headache and Psychiatric Variables

	CPAQ Total [‡]	CPAQ Pain Willingness [‡]	CPAQ Activity Engagement [‡]	PHQ-9	GAD-7
Headache Variables					
Migraine Diagnosis					
<i>Chronic Migraine (≥ 15 days/month)</i>	51.1 (18.9)	22.6 (8.5)	30.4 (13.8)	7.3 (6.1) *	4.1 (3.6)
<i>Episodic Migraine (<15 days/month)</i>	58.7 (17.6)	24.1 (8.7)	34.6 (11.3)	4.6 (4.2)	3.6 (4.4)
	<i>n</i> = 66	<i>n</i> = 71	<i>n</i> = 75	<i>n</i> = 82	<i>n</i> = 80
Average Headache Pain Intensity (0–10)	-.21	-.25	-.30 *	.15	.03
	<i>n</i> = 67	<i>n</i> = 72	<i>n</i> = 76	<i>n</i> = 82	<i>n</i> = 80
MIDAS					
<i>Severe Disability (≥ 21)</i>	48.7 (17.3) *	21.2 (8.2) *	27.8 (11.1) *	7.1 (5.2) *	5.3 (3.7) *
<i>Mild-Moderate Disability (<21)</i>	65.7 (11.0)	27.5 (6.8)	38.7 (10.0)	2.8 (2.7)	1.8 (2.4)
	<i>n</i> = 56	<i>n</i> = 58	<i>n</i> = 63	<i>n</i> = 67	<i>n</i> = 66
Psychiatric Symptoms					
Depression (PHQ-9)	-.48 *	-.40 *	-.46 *	-	-
	<i>n</i> = 67	<i>n</i> = 72	<i>n</i> = 76		
Anxiety (GAD-7)	-.37 *	-.32 *	-.30 *	.68 *	-
	<i>n</i> = 65	<i>n</i> = 70	<i>n</i> = 74	<i>n</i> = 83	

* Statistically significant;

[‡] For bivariate relationships between CPAQ scores and other variables, a Bonferroni-Holm correction for multiple comparisons was applied.

CPAQ = Chronic Pain Acceptance Questionnaire; MIDAS = Migraine Disability Assessment Score; ; PHQ-9 = Patient Health Questionnaire – 9; GAD-7 = Generalized Anxiety Disorder – 7.