Clinical Pain Research

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Pain acceptance and psychological inflexibility predict pain interference outcomes for persons with chronic pain receiving pain psychology

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Abstract

Objectives: Awareness (being present), acceptance, and engagement (committed action) are three dimensions of psychological flexibility. Understanding these in the context of chronic pain may identify treatment targets to help refine individual treatment. Our objective was to test the predictive capacity of three dimensions within the psychological flexibility model on the longitudinal trajectory of pain interference.

Methods: Patients receiving pain psychology treatment at a pain management center participated in this pragmatic clinical longitudinal study (n=86 with at least three assessments; Mean age=51 years; Gender=60 females, 26 males). Measures included the Five Facet Mindfulness Questionnaire (FFMQ-SF); Chronic Pain Acceptance Questionnaire (CPAQ-8); Psychological Inflexibility in Pain Scale (PIPS-12); and Committed Action Questionnaire (CAQ-8). The dependent variable was the Patient Reported Outcomes Information System (PROMIS) Pain Interference (PI). We used latent growth modelling to analyze scores assessed within 180 days of patient care.

Results: Psychological inflexibility (PIPS-12) and pain acceptance (CPAQ-8) measured at baseline predicted PI outcomes (n=86). PIPS-12 showed a direct relationship with pain interference (PI), where higher PIPS-12 scores predicted significantly higher PI mean scores on average across the study period (ρ=0.422, r^2=0.382) but also predicted significantly greater decreases in PI across time (ρ=−0.489, r^2=0.123). Higher CPAQ-8 scores predicted significantly lower PI mean scores on average across the study period (ρ=−0.478, r^2=0.453) but also significantly smaller decreases in PI across time (ρ=0.495, r^2=0.076). Awareness (FFMQ-SF) and engagement (CAQ-8) were not predictive of PI outcomes.

Conclusions: Patients who entered pain psychology treatment with lower pain acceptance and higher psychological inflexibility showed the largest reductions in pain interference across time. These results contribute towards a novel prognostic understanding of the predictive roles of an enhancing dimension and limiting dimension of psychological flexibility.

Keywords: acceptance; awareness; engagement; pain interference; predictive modelling; psychological flexibility.

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Introduction

Living with chronic pain constitutes a tremendous burden to individuals and society regarding reduced quality of life and productivity and increased healthcare costs [1]. While effect sizes are modest, cognitive-behavioral, and behavioral therapies can lessen this burden [2–4]. Current integrative theoretical models identify potential mechanisms of change underlying the benefits from these psychological approaches. These models aim to help us understand how

behavioral therapies work and may provide a path towards more optimal treatment and improved health outcomes [5]. Furthermore, using a theoretical moderation framework may better inform matching patients to specific treatments using baseline psychosocial characteristics that highlight limitations and strengths [6].

Psychological flexibility can be defined as the capacity to persist or to change behavior in a way that (1) includes conscious and open contact with thoughts and feelings, (2) appreciates what the situation affords, and (3) serves one's goals and values [7]. Psychological flexibility is a process-focused behavioural model that may explain the differences in health trajectories for people with chronic pain [7–9]. Awareness is one core enhancing dimension of psychological flexibility that relates to bringing non-judgmental attention to the present moment and is synonymous with "mindfulness" [10, 11]. Acceptance is a second core enhancing dimension that contrasts emotional avoidance. Engagement is a third core enhancing dimension that relates to promoting re-engagement in valued activities and includes "committed action" [7]. In contrast, cognitive fusion and avoidance (collectively referred to as psychological inflexibility), represent the limiting dimension of the psychological flexibility model. Collectively, strong evidence exists that increased psychological flexibility leads to improved functioning, well-being, and social connection [12].

Given that psychological flexibility contains multiple dimensions, we need to characterize better their shared and independent contributions in predicting commonly targeted health outcomes such as pain interference [13]. Pain interference is the extent to which pain adversely impacts engagement with physical, cognitive, emotional, and recreational activities [14, 15]. Evidence suggests that inadequate pain control, insomnia, and infrequent walking are predictive of pain interference in people with joint pain [16], however, evidence on the predictive capacity of awareness, acceptance, and engagement on pain interference outcomes is still being built [17]. Preliminary evidence suggests awareness can partially predict emotional pain-related interference in patients with primary headache [17] in addition to pain catastrophizing [18]. We also know that engagement can modestly predict physical function [9, 19], but the predictive capacity of engagement on pain interference is unknown.

Our knowledge of the psychological flexibility-pain interference relationship is predominantly based on studies designed to elucidate moderators and mediators of treatment effects [20–24]. For example, we know that pain acceptance can mediate the effects of psychological interventions on pain interference [20], and that psychological inflexibility can moderate the effect of Internet-based Acceptance and Commitment Therapy vs. no treatment on pain interference [22]. From a patient-treatment matching perspective, it would be helpful to know if baseline enhancing factors, like awareness, acceptance, and engagement and baseline limiting factors, like psychological inflexibility moderate treatment outcomes [6]. Gaining this knowledge from "real-world" settings, with participant samples drawn from patients seeking a variety of commonly employed pain psychology therapies is also needed. Therefore, the purpose of our study was to investigate the predictive capacity of enhancing and limiting dimensions within the psychological flexibility model on pain interference in patients receiving psychological treatment within a tertiary care pain clinic. Based on the available evidence [17, 20, 22], we expected that awareness, pain acceptance, and psychological inflexibility would predict pain interference outcomes. We did not propose a hypothesis for the predictive capacity of engagement on pain interference, as no prior evidence for this relationship has been established.

Methods

Participants

We enrolled patients receiving psychological treatment within a multidisciplinary outpatient pain management center in this prospective observational study. Hence, this study had broad inclusion criteria. The patients needed a pain medicine physician referral for pain psychology for inclusion in the study. The patients also needed to be adults (at least 18 years old) and be able to comprehend English to complete the self-reported questionnaires. The sample constituted persons with heterogeneous persistent pain conditions that were recruited to complete the self-report measures between January 2019 and December 2019. The pain management center is part of an urban, tertiary referral academic medical center in Northern California. This setting provides training to pain psychology postdoctoral fellows. All pain psychology care was delivered by pain psychologists (n=4) who held a doctoral level degree (PhD) and have completed or were receiving postdoctoral fellowship training in pain medicine. As a tertiary pain management referral center, most patients seen for pain psychology service receive an initial evaluation with treatment recommendations only. It is also common for a smaller portion of these patients to receive follow-up pain psychology treatment in addition to physical therapy assessment and treatment. It is this smaller portion of patients (approximately 20% of the total referrals) who received at least 3 pain psychology sessions over the course of 180 days that were included in this study. Some of the reasons for this practice pattern would include, for example, geographical distance from the clinic, or limited insurance coverage for pain psychology treatment.

Measures

Administration of all self-report measures. The design of this study incorporated a longitudinal assessment of prospective observational data, which was approved by the Institutional Review Board at the Stanford University School of Medicine and required informed consent. We collected self-reported measures (questionnaires) from patients receiving pain psychology treatment for each clinical encounter over 180 days. The patients completed all questionnaires prior to their pain psychology evaluation or follow up treatment appointment. A minimum of three time points were needed for inclusion in the analysis, which included an initial measure (pre-treatment), and two subsequent follow-up treatments. The time points of the collected self-reported outcomes between patients were asynchronous. In other words, patients did not provide follow-up assessment scores (time points 2 and 3) at structured intervals. If patients had more than 3 time points in the 180-day span, the 3 time points that were closest temporally were included in this analysis; the average duration of time elapsed between time points was between 45 and 50 days (Table 1). The time elapsed between time points 1 and 2 ranged from 5 and 147 days, and the time elapsed between time point 2 and time point 3 ranged from 21 to 174 days. These data were collected within a clinical environment, and hence, constituted a sample of convenience. Therefore, we recruited participants until we had a large enough sample to power our analyses; a post-hoc analysis was subsequently conducted to determine adequacy of power in the final sample. All data was collected electronically using a learning health care system platform, CHOIR (https://choir.standord.edu/) [25]. Sample items for each of the self-report measures described below are provided in Table 2.

Pain interference. Pain interference, our dependent variable, was assessed via the Patient Reported Outcomes Information System (PROMIS®) using a computerized adaptive test approach based on item response theory. PROMIS-Pain interference assesses the extent to which pain interferes with physical, cognitive, emotional, and recreational activities [26]. PROMIS instruments are calculated as raw total scores that are subsequently converted to t-scores, with a mean of 50 and standard deviation of 10. PROMIS-Pain interference is a psychometrically sound instrument with regards to reliability (0.96–0.99 for T-score range 50–80), construct validity, and discriminant validity across pain intensity, disability levels, and persistent conditions ($p<0.0001$) [26]. We chose pain interference as our primary outcome measure for several reasons. First, in accordance with recent consensus statements on chronic pain research [27], a meaningful assessment of the impact of chronic pain includes not only quantification of pain intensity but also broader measurement of pain-related interference in meaningful life activities. Second, pain-related interference or functional outcomes do not always follow the same trajectories of treatment response in individuals with chronic pain, illustrating the need to assess the variables independently [14]. Third, further studies have noted that improvements in pain-related functional measures may precede meaningful improvement in pain intensity [28, 29].

Table 1: The mean scores (±SD) for each of the measures of psychological flexibility and pain interference and mean time point. Scores presented as mean (SD).

Time point	1	2	3
Days after initial visit	–	45.6(31.0), n=86	94.5(37.0), n=74
PIPS-12	55.1(12.8), n=86	54.2 (13.0), n=85	51.4 (13.3), n=74
CPAQ-8	22.0(9.2), n=84	21.6(8.5), n=85	23.1, 8.7, n=74
CAQ-8	32.2(7.6), n=86	32.0(8.0), n=85	32.7(7.8), n=74
FFMQ-SF	82.9(12.6), n=86	83.5(13.8), n=85	83.2(12.2), n=74
Pain interference	66.3(5.3), n=86	66.1(6.8), n=86	63.8(7.0), n=74
Depression	58.6(7.7), n=86	57.7(9.1), n=86	55.6(9.1), n=74
Pain intensity	5.4(2.1), n=86	5.4(2.2), n=85	5.0(2.3), n=74

Table 2: Subscale and sample items of the self-reported measures reflecting psychological flexibility.

Measure	Subscale	Sample item
FFMQ-SF	Observation	I pay attention to physical experiences, such as the wind in my hair or sun on my face
	Description	I'm good at finding the words to describe my feelings
	Mindful actions	I find it difficult to stay focused on what's happening in the present moment
	Non-judgmental inner experience	I tell myself that I shouldn't be feeling the way I'm feeling
	Non-reactivity	I watch my feelings without getting carried away by them
PIPS-12	Avoidance	I avoid planning activities because of my pain
	Cognitive fusion	It is important to understand what causes my pain
CPAQ-8	Activities engagement	I am getting on with the business of living no matter what my level of pain is
	Pain willingness	I would gladly sacrifice important things in my life to control this pain better
CAQ-8		I can remain committed to my goals even when there are times that I fail to reach them

Abbreviations for measures: Five-Facet Mindfulness Questionnaire, Short Form (FFMQ-SF); Psychological Inflexibility in Pain Scale, 12-item version (PIPS-12); Chronic Pain Acceptance Questionnaire, 8-item version (CPAQ-8); Committed Action Questionnaire, 8-item version (CAQ-8).

Enhancing measures. We used three measures to assess the enhancing independent variables of *awareness*, *acceptance*, and *engagement*. Awareness was assessed using the total score from the 24-item Short Form version of the Five Facet Mindfulness Questionnaire (FFMQ-SF) [10, 30]. The FFMQ-SF has shown good reliability and validity across multiple populations, including people with chronic pain. The FFMQ-SF consists of five subscales – *observing*, *describing*, *acting with awareness*, *non-judging of inner experience*, and *non-reactivity*. We used the total score for all analyses (possible scores ranging from 24 to 120), and this omnibus score showed high internal consistency (α=0.887).

Acceptance was assessed using the Chronic Pain Acceptance Questionnaire (CPAQ-8) [31]. The CPAQ-8 has shown adequate reliability and validity in the chronic pain population [32]. The CPAQ-8 is

computed as a total score ranging from 0 to 48, with higher scores indicating higher acceptance of pain, and includes subscales of *activities engagement* and *pain willingness*. We used the total score in our analyses. Engagement was assessed using the Committed Action Questionnaire (CAQ-8) [33]. The CAQ-8 is a reliable and valid measure for people with chronic pain and has been shown to be associated with pain-related and general acceptance, depressive symptoms, physical and social functioning, mental health, vitality, and general health [33]. The CAQ-8 does not contain subscales and is calculated as a total score ranging from 0 to 48, with higher scores indicating greater engagement. Internal consistency of the CPAQ-8 (α=0.874) and CAQ-8 (α=0.881) were high.

Other processes within the psychological flexibility model were not included in this study that could be considered enhancing measures. "Self-as context", for example, involves embodying a perspective of observing experiences rather than identifying with them, and can be measured with the Self Experiences Questionnaire [34]. "Cognitive defusion" involves discerning between thoughts and the individuals or events they describe [35]. We elected not to include these measures in this study as the Self Experiences Questionnaire has only preliminary validation, and the Cognitive Fusion Questionnaire has a high degree of overlap with pain acceptance.

Limiting measure. We used one measure to assess the limiting independent variable of *psychological inflexibility* using the Psychological Inflexibility in Pain Scale (PIPS-12) [36]. The PIPS-12 has shown adequate reliability and validity across chronic pain populations in multiple countries, and consists of two subscales, *avoidance of pain* and *cognitive fusion* [37]. PIPS-12 total scores can be computed and range from 12 to 84, with higher scores indicating greater levels of inflexibility in responding to pain. The PIPS-12 subscales and the CPAQ subscales (*activities engagement* and *pain willingness*) are significantly correlated [36]. The PIPS-12 showed high internal consistency (α=0.830).

Covariate measures. Pain intensity, depressive symptoms, age, and gender were included as covariate measures as these factors are known to influence treatment outcomes [38–40]. Pain intensity was assessed on an 11-point numerical rating scale for average pain intensity over the past 7 days from 0 to 10 (0=no pain; 10=worst pain imaginable), which is a common and validated metric for pain intensity in chronic pain populations [41]. Depressive symptoms were measured using a computer adaptive testing version of PROMIS Depression, which captures primarily affective and cognitive manifestations of depressive symptoms (e.g., sad, or depressed mood, hopelessness, anhedonia) [42]. We chose to include depressive symptoms as a study covariate because it has been shown to predict health outcomes irrespective of the chosen treatment [43]. Age was represented as a continuous variable in years and gender was represented using a binary categorical variable of male/female. We were not able to capture patients who may have a non-binary gender identity in this dataset.

Treatment

According to routine practices within the pain center, patients received psychology services from several in-house psychologists with specialized training in pain psychology interventions. Common pain psychology treatment approaches include pain neuroscience and self-management education, cognitive behavioural therapy, mindfulness and self-compassion training, acceptance and commitment therapy, and biofeedback training. The allocation of the treatment(s) delivered was based upon the clinical judgment of the pain psychologist (i.e., the balance of patient needs and preferences). The typical duration of treatment ranged from 4–12 weeks. Before participation in pain psychology treatment, participants received consultations with a pain physician to optimize analgesic medications and potentially receive interventional procedures. In contrast, some participants also received a physical therapist's consultation to optimize physical activity and exercise.

Statistical analysis

We used latent growth modeling (LGM) to test the predictive capacity of the three enhancing measures (FFMQ-SF, CPAQ-8, CAQ-8) and one limiting measure (PIPS-12) representing dimensions of the psychological flexibility model on the trajectory of pain interference outcomes across the 180-day observational period. As mentioned previously, we include pain intensity, depressive symptoms, age, and gender as covariates in the LGM as these factors are known to influence treatment outcomes and used the LGM to analyse the predictive effects of the four psychological flexibility measures in relation to pain interference. Models were specified using Mplus version 6.12 (Version 6.12, Los Angeles, CA: *Muthén & Muthén*) specified for an unrestricted model accounting for missing data (TYPE=MISSING h1) and utilizing a maximum likelihood estimator with robust standard errors using a numerical integration algorithm (ALGORITHM=INTEGRATION). Missing data were handled in listwise fashion. All clinical variables were within acceptable standards regarding normality: absolute values of skewness and kurtosis were less than 2 for all variables [44]. Three time points were collected for each patient, which consisted of the initial evaluation (time point 1), and subsequent treatments (time points 2 and 3) occurring within the 180-day specified study period. If a patient had more than 3 sessions within the 180-day period, then the three most proximal assessments were used in the estimated model.

Separate models were estimated utilizing initial scores on psychological flexibility indicators as predictors, along with demographic (age and gender) and clinical covariates (pain intensity and depressive symptoms), of latent factors representing the intercept (mean variance) and slope (change across time) derived from pain interference scores sampled across the 180-day study period. Intercept scores reflect average scores on pain interference at Time 1, and slope scores reflect average change in pain interference across the study period. In other words, the intercept refers to factors related to stable variance in pain interference across the entire time period, and the slope refers to factors related specifically to changes in pain interference. A benefit of implementing the LGM approach is the ability to estimate latent variables for slope and intercept separately. For any psychological flexibility indicator that showed a significant effect on the latent slope variables, these effects were depicted visually using a median split representing differential trajectories of groups with high/low levels of the flexibility indicator in pain interference scores across time.

As a final exploratory step, a combined model estimating the concurrent relationships of each predictor with pain interference slope and intercept latent variables was estimated. In order to adjust for multiple comparisons inherent in the large number of estimated parameters in SEM, we applied a Benjamini–Hochberg false discovery rate (FDR) approach to adjust p-values [45]. This approach utilizes a rank ordering of estimated parameters according to probability values and then applies a cut-off computed using the product of the *a priori*

alpha (α=0.05) and a ratio of the rank position of the parameter divided by the total number of parameters. Significance was determined if the estimated p-value fell below the rank order p-value cut-off estimated by this approach. Computation of descriptive statistics were performed using SPSS (Windows version 20, Chicago, IL, USA). A post-hoc power analysis was conducted using the LIFESPAN program [46]. Power for each LGM was estimated post-hoc using 1000-draw Monte Carlo estimation with the final study sample (n=83) with 2 specified degrees of freedom. Power was found to be adequate for all estimated models (power estimates ranging from 0.843 to 0.969). Effect sizes are represented for all significant relationships in the form of r^2 metrics. These r^2 estimates represent the proportion of variance accounted for in the latent intercept and slope variables by the predictor without covariates included in the model.

Results

Demographics

Between January 2019 and December 2019, 457 people with chronic pain completed the included self-report questionnaires (the Pain Psychology CHOIR surveys). Of these, 86 patients had at least three assessments over 180 days and were considered for the longitudinal analysis. The second and third assessments tended to occur approximately 45 days apart. Regarding age and gender identification, the patient sample included a mean age of 51.1 years (SD=15.3) and gender identity of female (n=60) and male (n=26). Regarding race, participants identified as Caucasian or White (n=65), Hispanic or Latino (n=10), Unknown or Other (n=7), Asian (n=2), and African American/Black (n=2). Dropout analyses suggested no significant differences in any demographic or study variable between those patients included in the sample and those who did not provide sufficient data to be included in the analysis.

The predictive capacity of enhancing dimensions of psychological flexibility

The mean scores (±SD) for the enhancing dimensional measures of psychological flexibility – awareness, acceptance, and engagement, and pain interference and mean time point are presented in Table 1. Initial scores in each of these psychological flexibility indicators were used as predictors of pain interference changes in the latent growth models; all analyses were conducted controlling for the effects of pain intensity, depressive symptoms, age, and gender.

Awareness as assessed with the Five Facet Mindfulness Questionnaire (FFMQ), and *engagement* as assessed with the Committed Action Questionnaire (CAQ-8) were not predictive of pain interference outcomes. However, *acceptance* as assessed with the Chronic Pain Acceptance Questionnaire (CPAQ-8) was predictive of pain interference outcomes. Here, pain acceptance showed an inverse relationship with pain interference, where higher CPAQ-8 scores predicted significantly lower pain interference mean scores on average across the study period (ρ=−0.478, r^2=0.453) but also significantly smaller decreases in pain interference across time (ρ=0.495, r^2=0.076), Figure 1. The trajectories in pain interference across time between patients with high and low pain acceptance are displayed in Figure 2.

The predictive capacity of the limiting dimension of psychological inflexibility

The limiting dimension of psychological inflexibility, as assessed with the Psychological Inflexibility in Pain Scale (PIPS-12) showed a direct relationship with pain interference, where higher PIPS-12 scores predicted significantly higher pain interference mean scores on average across the study period (ρ=0.422, r^2=0.382) but also predicted significantly greater decreases in pain interference across time (ρ=−0.489, r^2=0.123), Figure 3. The trajectories in pain interference between patients with high and low psychological inflexibility (according to a median split) are displayed in Figure 4.

Combined model predicting pain interference

When a combined model was estimated examining the concurrent relationships between all examined predictor variables and pain interference, most paths were found to be non-significant except for the path from pain acceptance (CPAQ-8) to the pain interference intercept latent variable (ρ=−0.587, p<0.001).

Discussion

The purpose of our study was to investigate the predictive capacity of enhancing and limiting dimensions within the psychological flexibility model on a commonly targeted health outcome (pain interference) in patients receiving psychological treatment within a tertiary care pain clinic. Our hypothesis that awareness would predict pain interference was not supported, however, our hypotheses that pain acceptance and psychological inflexibility would

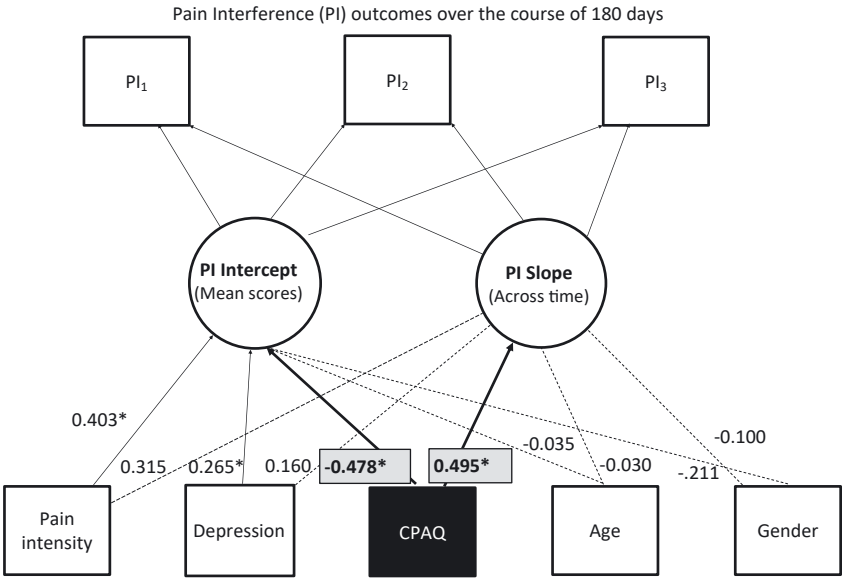

Figure 1: Latent growth model of the predictive effects of the Chronic Pain Acceptance Questionnaire (CPAQ-8) on Pain Interference (PROMIS PI). CPAQ-8 and PI showed an inverse relationship, where higher CPAQ-8 scores predicted lower PI mean scores (PI intercept) and greater PI negative slope trends across time (PI slope). CPAQ-8 scores are a total for the subscales for pain willingness and activity engagement. Covariates of pain intensity (PROMIS), Depression (PROMIS), age, and gender were included in the model. $PI_{1\text{-}5}$ denotes observation time points over the course of 180 days of pain psychology care. Note: Significant after correction for multiple comparisons; Sample size = 90.

predict pain interference outcomes was supported. Results indicated that patients who entered pain psychology treatment with lower pain acceptance and higher psychological inflexibility showed the greatest decreases in pain interference across time. These results contribute towards a novel prognostic understanding of the predictive roles of an enhancing and limiting dimension of psychological flexibility.

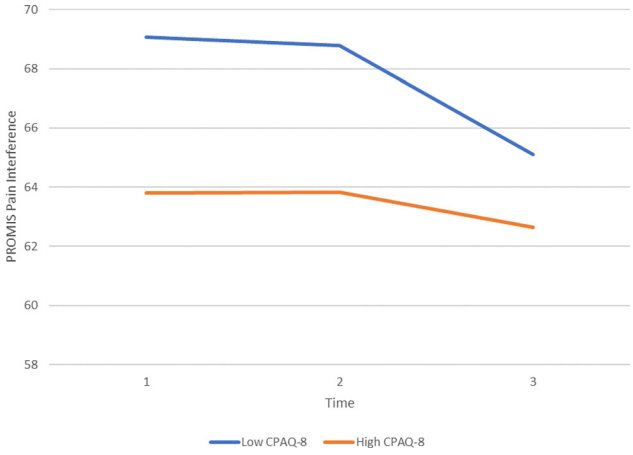

Figure 2: Trajectories in pain interference between patients with high- and low-pain acceptance. Pain Interference measured with PROMIS. Pain acceptance measured with the Chronic Pain Acceptance Questionnaire (CPAQ-8).

Enhancing dimensions of psychological flexibility

Acceptance. One key finding was that pain acceptance altered the trajectory of pain interference across time, a finding that remained robust even when covariates of pain intensity and depressive symptoms were included in the model. This finding further suggests that those most likely to respond to the behavioral treatment were those who entered pain psychology treatment with lower levels of pain acceptance. Prior studies have shown that pain acceptance plays a mediating role on pain interference [20] and physical function [47], however, this is the first study to our knowledge that has shown baseline pain acceptance *predicts* pain interference for patients seeking treatment in a tertiary pain care setting.

One interpretation of these findings is that the referring provider(s) to pain psychology consultation are identifying subtle or overt features of low pain acceptance during the clinical encounter, which is then further prompting the physician to refer the patient to pain psychology care. A second interpretation is that low pain acceptance is not a predominant feature clearly identified in the patient's pain experience and clinical presentation yet is nonetheless a predictive feature for patients who express greater improvements in pain interference across time. A third interpretation is that the construct of acceptance is a general process that is present in psychological treatment and one which improves as patients positively respond to their

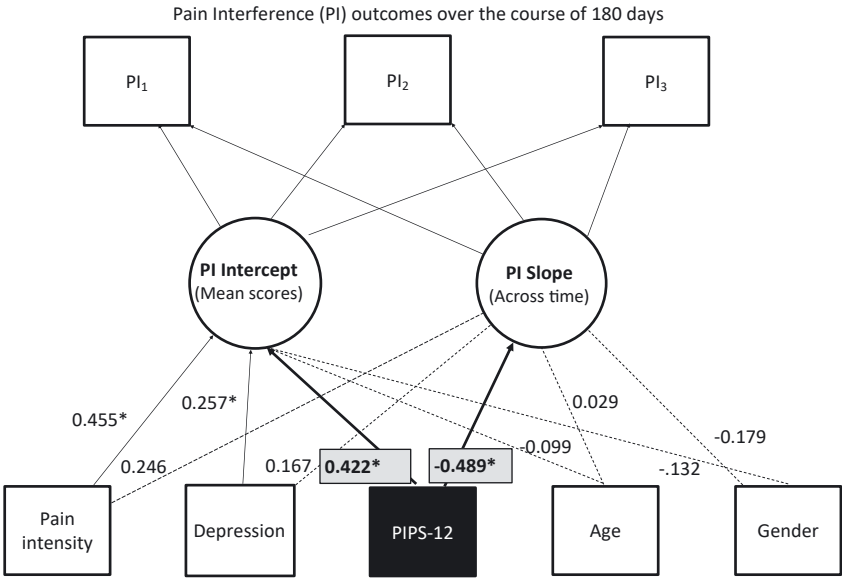

Figure 3: Latent growth model of the predictive effects of the Psychological Inflexibility in Pain Scale (PIPS-12) on Pain Interference (PROMIS PI). PIPS-12 and PI showed a direct relationship, where higher PIPS-12 scores predicted higher PI mean scores (PI intercept) and greater PI positive slope trends across time (PI slope). PIPS-12 scores are the total of the subscales for avoidance and cognitive fusion. Covariates of pain intensity (PROMIS), Depression (PROMIS), age, and gender were included in the model. $PI_{1\text{-}5}$ denotes observational time points over the course of 180 days of pain psychology care. Note: * = Significant after correction for multiple comparisons; Sample size = 86.

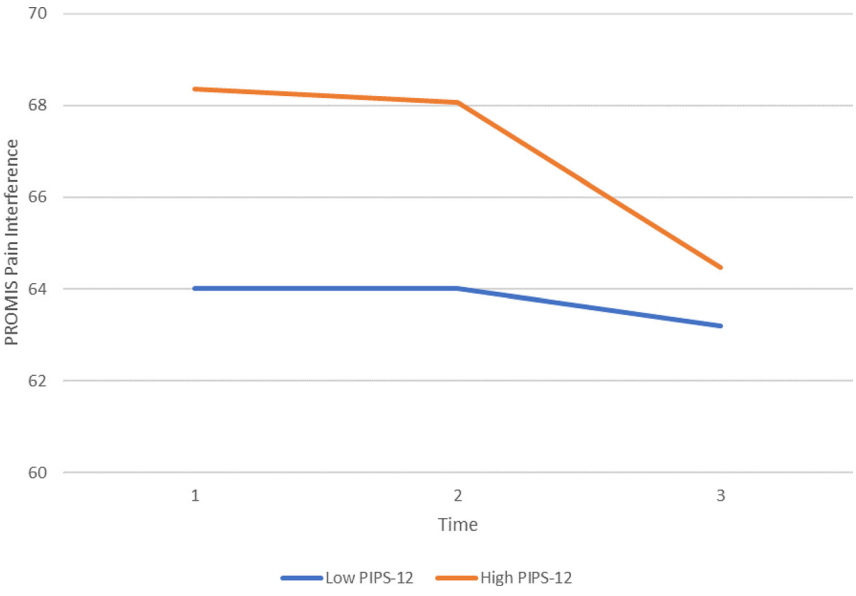

Figure 4: Trajectories in pain interference between patients with high- and low-psychological inflexibility. Pain interference measured with PROMIS. Psychological inflexibility measured with Psychological Inflexibility in Pain Scale (PIPS-12).

psychological treatment. While pain acceptance has demonstrated some ability to predict functioning in people with chronic pain [48, 49], predictive modelling in the context of identifying treatment responders will remain limited given the inherent heterogeneity and bio-psychosocial complexity at the patient and therapist levels. Furthermore, while neuroscience supports the view that we have the ability to change how our minds work and how we act or behave, floor and ceiling effects need consideration. In other words, where one begins in terms of "mindset" at the initiation of pain psychology treatment may affect how much one can improve in "mindset" at the conclusion of treatment.

Awareness. Contrary to prior research findings [17], our study did not find a significant *predictive* capacity of awareness on pain interference outcomes. We are unable to explain this discrepancy, however, we acknowledge that there are differences in the self-report measures and study population between studies. For example, Namjoo et al., used the Brief Pain Inventory and Mindful Attention Awareness Scale and investigated patients with primary headache in a hospital setting in Iran. While the evidence is not conclusive about the disparity in sensitivity between PROMIS Pain Interference and the Brief Pain Inventory, it is possible that the PROMIS Pain Interference is less sensitive to change [50, 51]. Dosage, adherence, and type of

mind training (e.g., meditation) are also known to influence the effectiveness of awareness practice [52, 53]. Although not identified or monitored in our study, the types of psychological treatment prescribed or practiced during clinical sessions or home practice could have played a role in the lack of predictive capacity of awareness on pain interference.

The predictive capacity of awareness may depend on the outcome variable. For example, while our study focused on pain interference, another study focused on pain catastrophizing and showed that awareness was predictive of this outcome variable [18]. Additionally, the predictive capacity of awareness may only be observed for mindfulness-based therapies. Our findings may also be explained by the fact that participants in our study were exposed to a broad range of pain psychology treatments. Some of these treatments may have contained no or little emphasis on the cultivation of awareness but contained a higher emphasis on the cultivation of self-efficacy.

Engagement. Our results illustrated that engagement, the persistence in values-based and goal-directed behavior, did not significantly *predict* pain interference outcomes. Other studies have also explored the relationship between engagement and other self-reported outcomes that may have a relationship with pain interference, such as physical health, physical function, and physical disability. One of these studies showed that engagement, as assessed with the Chronic Pain Values Inventory, did not impact physical disability [23]. Another study showed that engagement modestly predicted physical function [9, 19]. While physical health, physical function, and physical disability may be related to pain interference, they each have unique psychometric properties and longitudinal trajectories [14].

Limiting dimension of psychological inflexibility

A second key finding was that psychological inflexibility, as assessed with the Psychological Inflexibility in Pain Scale (PIPS-12), further altered the trajectory of pain interference across time. This is the first study to our knowledge that has examined the predictive capacity of psychological inflexibility on pain interference outcomes for patients seeking treatment in a tertiary pain care setting. The same interpretations which were highlighted earlier pertaining to pain acceptance could apply here, for psychological inflexibility, as well. One of these studies has shown that the avoidance subscale of the PIPS was highly correlated with and contributed significantly to the prediction of both subscales of the CPAQ [36], suggesting some convergence between these measures. In other words, one could consider activity avoidance as the flip side of pain acceptance. However, another study has shown that PIPS measures different processes than the CPAQ [54], suggesting some divergence between these measures.

Limitations

One limitation of this study is related to the nature of the data in terms of asynchrony and loss. A second limitation is related to the data heterogeneity in terms of the patient and treatment. A third limitation is related to the study design in terms of a lack of a control condition.

Data asynchrony and loss. These data were collected within a clinical setting where patients received pain psychology consultation and treatment under the care of multiple pain psychologists. This inherently provides asynchronous data regarding the different time points of assessment between patients. Hence, while the data points were constrained within a 180-day window, the data were not structured in the same manner as a randomized controlled trial or prospective observational study with typical study outcome endpoints or milestones (i.e., 1-month, 3-month, 6-month). Given the inherent structural demands of the LGM, data were structured in a way that emulated these structured time points, which inaccurately represents the asynchronous nature of the CHOIR assessments. Although this step was necessary to estimate the LGM models, it should be considered a limitation and any conclusions about the time frame of treatment response should be drawn with this limitation in mind.

Due to the nature of using a clinical dataset, there is also considerable loss of data. Our data showed a higher consistency in initial visit assessments and lower consistency in follow-up assessments, which is reflective of the common clinical practice for this tertiary, interdisciplinary pain management referral center. Hence, there may be unique aspects of the individuals who continued to receive follow up treatment compared to those individuals who stopped receiving pain psychology treatment which we did not measure, such as motivation to change, treatment expectations, and the patient-provider connection. Finally, these data lack information about referral success (i.e., how many were referred but never seen) or those that were seen but did not complete all assessments.

Data heterogeneity. These data are representative of patients who are seeking clinical treatment and may not be representative of a community-based population. The patient population in our study was highly heterogeneous in

terms of the chronic pain condition for which they were seeking treatment. While this diversity in the patient sample provides high external validity, it also has the potential to reduce precision or applicability to individuals within this diverse group. This may be relevant in light of some evidence [53] that changes in bodily pain, health-related quality of life, and psychological well-being for patient receiving a Mindfulness Based Stress Reduction program vary based on the chronic pain condition (i.e., larger treatment effect size in arthritis vs. fibromyalgia). We can also equally state that there is not a specific reason *a priori* to believe that the constructs of psychological flexibility would not be applicable across a variety of pain classifications or phenotypes. While this has not been empirically tested, psychological flexibility may be conceptualized as a transdiagnostic factor [55].

Finally, while all patients received evidence-based behavioural therapy, the dose and specific therapeutic techniques and dose and type of mind training (a.k.a., meditation) prescribed for home practice were varied. This is relevant given that we know adherence to meditation practice influences outcomes [53], and that this is a common modality prescribed in pain psychology. In contrast, there is also evidence supporting the view that changes in awareness and pain acceptance were not significantly different between individuals receiving two common pain psychology treatments – Cognitive Behavioural Therapy and Mindfulness Based Stress Reduction [56]. Additionally, a systematic review and meta-analysis has previously concluded that Acceptance and Commitment Therapy does not necessarily contribute to larger effect sizes than Cognitive Behavioural Therapy [57]. Furthermore, in addition to pain psychology treatment, some of these patients may have received less or more intensive interdisciplinary treatment (e.g., medical, physical therapy, social work), further adding to the data heterogeneity. This is relevant because intensive interdisciplinary treatment has been shown to improve physical health and function [58, 59].

Study design. More rigorous study designs are warranted, such as an RCT informed by an expanded set of psychological flexibility indices and further informed by Acceptance and Commitment Therapy. A treatment as usual control condition would potentially control for the possibility of regression to the mean. Observational, prospective studies which provide more detailed pain classification and phenotyping within a more specified pain population (i.e., chronic low back pain) would potentially allow for higher control of data quality and reduced variability in results. Furthermore, increased demographic diversity, and monitoring of the treatment dosage and frequency would improve data quality and retention, and allow for more detailed interpretation of the data.

Future directions

While our study provided preliminary predictive findings related to key enhancing and limiting dimensional profiles within the psychological flexibility model that might benefit the most in terms of improvement in pain interference, future investigations using alternative study designs (as mentioned above), an expanded set of psychological flexibility measures (Multidimensional Psychological Flexibility Inventory), and a larger sample size could build upon these findings. Regarding the expansion of measures, there are additional processes specific to psychological flexibility (cognitive fusion/defusion, self-as-context, values) and non-specific to psychological flexibility (i.e., treatment expectations, patient-provider connection) that were not measured in this study which could further explain the predictions we observed. For example, self-as-context, another construct with the psychological flexibility model, is associated with changes in pain interference [60]. A more recently published study has demonstrated validity of a measure which represents all facets of psychological flexibility in a chronic pain population, termed the Multidimensional Psychological Flexibility Inventory [61].

Furthermore, while equanimity [62], and self-compassion [63] are not explicit measures within the psychological flexibility model, these mindfulness-based processes may be correlated with the awareness component of the psychological flexibility model, and help to further explain changes in physical health and psychological wellbeing outcomes.

Future research could further incorporate additional limiting, activating, and enhancing approaches into the model [6] to provide more precise patient-treatment matching, and include additional constituents of well-being such as insight, purpose, and social connection [64]. The integration of qualitative pain narrative reports [65], along with quantitative self-report measures, and non-self-report measures (i.e., psychophysical, physical capacity, neurophysiological data) would provide a more comprehensive assessment of pain-related suffering, elucidate pain mechanisms, and further the progress of personalized medicine.

Conclusions

Patients who entered pain psychology treatment with lower pain acceptance and higher psychological inflexibility showed the largest reductions in pain interference

across time. These results contribute towards a novel prognostic understanding of the predictive roles of an enhancing dimension and limiting dimension of psychological flexibility. Therefore, matching patients with specific therapies aimed at cultivating pain acceptance and limiting cognitive fusion and avoidance may hold therapeutic value in lessening the interference of various dimensions of the patient's life.

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