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Authors

Trost, Zina
Strachan, Eric
Sullivan, Michael
et al.

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Heritability of Pain Catastrophizing and Associations with Experimental Pain Outcomes: A Twin Study

Zina Trost, Ph.D.¹, Eric Strachan, Ph.D.², Michael Sullivan, Ph.D.⁴, Tine Vervoort, Ph.D.⁵, Ally R. Avery³, and Niloofar Afari, Ph.D.⁶

¹Department of Psychology, University of North Texas, Denton, TX

²Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA

³Department of Epidemiology, University of Washington, Seattle, WA

⁴Department of Psychology, McGill University, Montreal, QC, Canada

⁵Department of Experimental-Clinical and Health Psychology, Ghent University, Belgium

⁶VA Center of Excellence for Stress and Mental Health and Department of Psychiatry, University of California, San Diego, San Diego, CA

Abstract

The current study employed a twin paradigm to examine the genetic and environmental contributions to pain catastrophizing as well as the observed association between pain catastrophizing and cold pressor task (CPT) outcomes. Male and female monozygotic ($n=206$) and dizygotic twins ($n=194$) from the University of Washington Twin Registry completed a measure of pain catastrophizing and performed a CPT challenge. As expected, pain catastrophizing emerged as a significant predictor of several CPT outcomes, including cold pressor immersion tolerance, pain tolerance, and delayed pain rating. The heritability estimate for pain catastrophizing was found to be 37% with the remaining 63% of variance attributable to unique environmental influence. Additionally, the observed associations between pain catastrophizing and CPT outcomes were not found attributable to shared genetics or environmental exposure, suggesting a direct relationship between catastrophizing and experimental pain outcomes. This study is the first to examine the heritability of pain catastrophizing and potential processes by which pain catastrophizing is related to experimental pain response.

1. Introduction

Pain catastrophizing emerges as one of the most robust predictors of adverse pain outcomes [1–4]. Numerous studies document the association between pain catastrophizing and adverse pain outcomes in the context of acute and chronic pain. High levels of catastrophizing are associated with heightened pain intensity, psychological distress, and disability [1, 2, 5, 6].

Correspondence concerning this paper should be addressed to Niloofar Afari, Ph.D., 9500 Gilman Drive, 0737, La Jolla, CA 92093; 858-534-2670; nafari@ucsd.edu.

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Increasingly, researchers have turned their attention to the origins of pain catastrophizing and mechanisms through which pain catastrophizing impacts pain outcomes [7–10].

Cognitive-behavioral models have been the dominant conceptual frameworks invoked to explain the ontology and mechanism of action of pain catastrophizing. It has been suggested that, as a function of a learning history characterized by heightened pain experience, those with high level of catastrophizing may develop “pain schema” containing excessively negative information about pain-related experiences, and pessimistic beliefs about pain or the ability to cope with pain [6, 11]. These schema may then influence emotional or cognitive functioning in a manner that leads to heightened pain experience [12]. Conversely, evidence that catastrophizing appears relatively early in life and predicts pain outcomes in the absence of prior pain experience points to the potentially antecedent nature of pain catastrophizing [6, 11].

A few recent studies provide indirect evidence for a familial or genetic contribution to pain catastrophizing. For example, one study found that parental pain catastrophizing accounted for 20% of the variance in pain catastrophizing reported by their adult children [13]. Another study found a strong correlation between child and parent catastrophizing in a sample of young schoolchildren [14]. Further, both child and parental pain catastrophizing predicted children’s attention and avoidance behavior in response to an experimental pain task [14]. Similar associations have been observed among parents and adolescents [15]. A handful of studies also point to a role for catechol-O-methyltransferase (COMT) in pain catastrophizing. One study implicated the COMT gene in pain catastrophizing within a fibromyalgia sample [16], and another reported findings suggesting that interaction between pain catastrophizing and specific genotype activity (i.e., COMT) might influence pain responses [17].

The above findings raise the possibility that pain catastrophizing may be a partially heritable trait and may interact with known genetic markers to influence pain response [18]. However, to date no study has specifically examined the heritability of pain catastrophizing or the underlying genetic associations between catastrophizing and pain outcomes. The primary aim of this study was to examine the heritability of pain catastrophizing using twin pairs from the University of Washington Twin Registry. Analyses examined the proportion of variance in catastrophizing accounted for by additive genetic, common environmental, and unique environmental effects. A second exploratory aim examined whether the association between pain catastrophizing and pain responses to a cold pressor task (CPT) was partially attributable to shared genetics and/or common environmental exposures. This exploratory aim addresses potential processes by which pain catastrophizing may be related to pain responding, either directly or through shared genetic and/or common environmental origins.

2. Methods

2.1 Participants

Same-sex twin pairs from the University of Washington Twin Registry (UWTR) were recruited specifically for a study to examine the psychosocial, demographic, and clinical factors associated with experimental pain sensitivity. The UWTR is a community-based

sample of twins drawn from information gathered by the Washington State Department of Licensing. A detailed description of Registry participant recruitment procedures are described elsewhere [19, 20]. Same-sex twin pairs who were 18–65 years old were eligible for the present study. Based on those criteria, potential participants were randomly selected from the UWTR. A study coordinator contacted twins individually to screen them for study eligibility. All screening information was reviewed by the study physician to determine if potential participants were healthy enough to participate in the study. Potential participants with a medical condition that could interfere with study measurements, such as an autoimmune disorder, were excluded from the study. Participants who were taking oral steroids, opiates, or other prescription pain medications on a regular basis were excluded from the study. Additional exclusions included a BMI of $< 18.5 \text{ kg/m}^2$, pregnancy, neuropathy, blindness, deafness, or missing limbs.

A total of 752 individuals were screened for participation in the study. Of those, 75 individuals (one or both of a twin pair) did not meet inclusion criteria due to pain or immune-modulating medications ($n=33$), BMI ($n=14$), current or anticipated pregnancy ($n=10$), neuropathy ($n=16$), and ongoing cancer treatment ($n=2$), resulting in 278 eligible twin pairs. Of eligible twin pairs, 77 pairs were unable participate due to scheduling issues (e.g., inability to reach one of the twins, inability to coordinate appointment time, cancelling too many visits). The final sample included 400 basically healthy male and female twins (200 twin pairs). As would be expected in a community sample of otherwise healthy adults, 49 individuals reported some chronic pain, primarily headache and back pain. All twins in the sample were reared together. Participants came into the UWTR laboratory for a 4-hour visit which included the completion of a battery of self-report instruments, an array of experimental pain tasks, and biological sample collection. Participants were instructed not to take any pain medications for the 24 hours prior to the laboratory visit. Written informed consent was obtained from each participant and all procedures were approved by the University of Washington Institutional Review Board.

2.2 Assignment of Zygosity

Zygosity was determined by using either the AmpFISTR[®] Identifiler[®] Plus PCR Amplification Kit or the PowerPlex[®] 16 HS System. The two protocols are nearly identical and all assays were conducted per manufacturer's instructions at the University of Washington Center for Clinical Genomics.

2.3 Pain Catastrophizing

The Pain Catastrophizing Scale (PCS) [23] was used as a measure of catastrophic thinking about pain. The PCS contains 13 items describing different thoughts and feelings that individuals may experience when they are in pain. The current study used the standard instructional set accompanying the PCS measure (see http://sullivan-painresearch.mcgill.ca/pdf/pcs/Measures_PCS_Adult_English.pdf for exact wording). Specifically, participants were asked to reflect on past painful experiences, and to indicate the degree to which they experienced each of 13 thoughts or feelings when in pain using a 5-point scale ranging from (0) *not at all* to (4) *all the time*. Total PSC score can range from 0

to 52. The PCS has been shown to have excellent psychometric properties [21–23]. Internal consistency for the current sample was high (Cronbach's alpha coefficient = .91).

2.4 Cold Pressor Task (CPT) and Experimental Pain Responses

The cold pressor test (CPT) was used to measure evoked pain sensitivity along several domains. The device was a 12-L container filled with water and ice maintained at 1–2 degrees Celsius by constant circulation with an internal pump [24]. Participants were asked to immerse their non-dominant hand in the water up to the wrist. The maximum exposure to the cold pressor was limited to 300 seconds. The temperature in the testing room was maintained by a thermostat to ensure constant air and water temperature.

Participants' behavioral and self-report responses to the CPT were recorded. Specifically, participants were asked to indicate the onset of pain experience; the latency from immersion to indication of pain onset (in seconds) was recorded as participants' *CPT Pain Threshold*. Participants were asked to withdraw their hand when the pain became intolerable; latency from hand immersion to hand withdrawal was recorded as *CPT Immersion Tolerance*. We also calculated participants' latency to hand withdrawal following indication of pain onset by subtracting Pain Threshold from Immersion Tolerance; this parameter has been conceptualized as participants' ability to tolerate actual pain experience associated with the CPT and was recorded as *CPT Pain Tolerance* [24]. Finally, participants were asked to rate their pain intensity at three time points during the procedure – at the point they indicated pain onset (*CPT Threshold Pain Rating*), when they withdrew their hand from the CPT (*CPT Immersion Tolerance Pain Rating*), and at 15 minutes following hand withdrawal (*CPT Delayed Pain Rating*). The *CPT Delayed Pain Rating* asked participants to indicate their *current* pain intensity, and allowed examination of participants' return to baseline pain status. Ratings were made on a 100 mm visual analog scale.

2.5 Data Analytic Approach

Descriptive statistics were computed for participant demographic variables and CPT responses as means and standard deviations for continuous measures and percentages for categorical measures; descriptives were computed for the entire sample and separately for monozygotic (MZ) and dizygotic (DZ) twin pairs. Generalized estimating equations (GEE) were then used to examine the association of PCS score with the six CPT outcome variables listed above. We refer to this as the “overall phenotypic associations” in that we are looking for an association between the pain catastrophizing phenotype (indexed by participants' PCS score) and the various CPT phenotypes (indexed by participants' responses to the CPT). GEE analyses are most appropriate for twin data analyses as they take into account the correlated data within twin pairs. We also used Spearman's rho, accounting for non-normal data to examine correlations amongst the CPT variables.

Quantitative genetic techniques rely on the assumption that MZ twins share a common set of genes while DZ twins share approximately half their genes, thus facilitating the study of genetic and environmental contributions to pain experience. To examine the heritability of pain catastrophizing, we used structural equation models to break the total variance in the total PCS score into additive genetic (*A*), common environment (*C*), and unique

environment (*E*) components. This is typically referred to as the “ACE” model. In this model, *A* represents the additive effects of alleles at the relevant genetic loci and is assumed to be perfectly correlated in MZ pairs while being correlated at 0.5 in DZ pairs; *C* represents environmental influences that make twins raised together more similar and is assumed to be perfectly correlated for both MZ and DZ pairs; *E* represents experiences that are unique to each twin, are uncorrelated for both MZ and DZ pairs, and that therefore drive within-pair differences (*E* also includes measurement error). When the MZ correlation is more than twice the magnitude of the DZ correlation, an alternative model can be fit where the *C* component is dropped and instead non-linear genetic effects labelled *D* are included, resulting in an ADE model; *D* denotes “dominance” genetics -- the major non-linear genetic effect [25]. Although (as will be described below) we found that the MZ correlations were more than twice the magnitude of the DZ correlations for pain catastrophizing and other outcomes in the current study, we elected not to fit ADE models because we were more interested in the total effects of genetics (i.e., total heritability) than whether the heritability is *A* alone or *A*+*D*.

Since it was necessary to document significant *A* or *C* variance in PCS as well as the CPT variables before addressing our exploratory aim, we first examined the within-pair Pearson correlation coefficients stratified by zygosity for each of the CPT variables with significant PCS/CPT associations. If the MZ correlations were larger than the DZ correlations, we conducted ACE modeling similar to that described above. Those CPT variables with significant *A* or *C* components were then used in the “quasi-causal” models to address our exploratory aim of examining whether observed associations between pain catastrophizing and pain responses were partially attributable to shared genetics and/or common environmental exposures [26]. Structural equation modeling was used to estimate the phenotypic association of PCS with CPT variables controlling for shared genetics (*A*) and common environment (*C*) [27]. As noted above, MZ twins share 100% of their genes and DZ twins share on average 50% of their genes. In addition, MZ and DZ twins reared together share all of their common environments (e.g., parental SES, parental educational background, neighborhood environments). Therefore, twin studies can statistically adjust for all measured and unmeasured genetic and environmental similarities that make MZ twins similar to one another. Any remaining twin differences in the MZ twins are thus deemed direct or quasi-causal. The term quasi-causal refers to the use of twin data to rule out important confounds in the phenotypic association between two variables related to shared genetics and developmental history. This is the best substitute we have for the impossible alternative of randomly assigning people to levels of pain catastrophizing in a true experiment of pain response. Using this rationale, any observed phenotypic association that remains significant in these quasi-causal models suggests a direct association between PCS and CPT outcomes. Any phenotypic association that would be attenuated and/or non-significant controlling for *A* and *C* suggests confounding -- i.e., that the phenotypic association is attributable at least in part to shared genes and/or environment. Figure 1 shows the general path diagram for these analyses (the model is shown for only one twin in a pair). In this figure, the phenotypic regression (*p-reg*) is the association between variables of interest, controlling for the effects of shared genetics (*a-reg*) and common environment (*c-reg*). Model fit was assessed using root mean square error (RMSEA) with a cut-off of .08.

The structural equation models were analyzed in Mplus Version 6 [28]. We used the MLR estimator in all models that included variables with non-normal distributions. The MLR estimator provides robust standard errors that are adjusted for the degree of non-normality in the data. All other analyses were done in PASW Statistics 18 (Release 18.0.0, July 30, 2009).

3. Results

3.1 Sample Characteristics and CPT Outcomes

Participants included 53 pairs of MZ female twins (FMZ, $n = 106$), 50 pairs of MZ male twins (MMZ, $n = 100$), 53 pairs of DZ female twins (FDZ, $n = 106$), and 44 pairs of DZ male twins (MDZ, $n = 88$). Sample characteristics and CPT outcomes for the entire sample and by zygosity are provided in Table 1. The average age was 28.8 ($SD = 12.3$) years for the entire sample and the majority of participants identified as White (80%). Aside from age where DZ twins were slightly but significantly older than MZ twins, there were no differences on any of the demographic characteristics, PCS score, and CPT pain outcomes between MZ and DZ twin pairs. CPT Immersion Tolerance was right censored (42 individuals reached 300 seconds without withdrawing their arms) which also affected the distribution of CPT Pain Tolerance. CPT Pain Threshold was right skewed. The CPT Pain Rating variables were normally distributed.

3.2 Association between Pain Catastrophizing and CPT Outcomes

Table 2 shows the overall phenotypic association between PCS and the six CPT pain outcomes. Participants' PCS score showed the strongest associations with outcomes related to endurance of painful stimuli (i.e., Immersion Tolerance and Pain Tolerance). Specifically, higher levels of catastrophizing were significantly associated with shorter Immersion and Pain Tolerance. For self-reported pain ratings, participants' PCS score only showed a significant positive association with CPT pain ratings collected 15 minutes following completion of the CPT procedure (i.e., CPT Delayed Pain Rating) in that higher levels of catastrophizing were associated with higher delayed ratings of pain. As expected, The CPT outcome variables were significantly correlated with each other (Table 3).

3.3 Heritability Estimates for Pain Catastrophizing

The top half of Table 4 shows the within-pair correlations of PCS by zygosity and the estimates of heritability (A) and unique environmental contributions (E) to participants' PCS score from the ACE models. The PCS scores showed a significantly higher correlation within MZ twin pairs ($r = .45, p < .05$) as compared to DZ twin pairs where the correlation was non-significant ($r = .04, ns$). The higher correlation among MZ twins is suggestive of heritability and indeed, the heritability estimate for catastrophizing (A) was found to be 37% with the remaining 63% of variance in PCS attributable to unique environmental influence (E).

3.4 Heritability Estimates for CPT Pain Responses

To pursue our second aim, we next examined whether CPT Immersion Tolerance, CPT Pain Tolerance, and CPT Delayed Pain Rating showed evidence of heritability. The bottom half

of Table 4 shows both the within-pair correlations and estimates of heritability and unique environmental contributions to the CPT responses. Participants' CPT Immersion Tolerance showed a significantly higher correlation within MZ twin pairs ($r = .56, p < .05$) as compared to DZ twin pairs ($r = .22, p < .05$). Similarly, participants' CPT Pain Tolerance showed a higher correlation within MZ twin pairs ($r = .53, p < .05$) than DZ twin pairs ($r = .21, p < .05$). For CPT Immersion Tolerance and CPT Pain Tolerance, heritability estimates (A) were found to be 55% and 52%, respectively, while unique environmental contributions (E) were found to be 45% and 48%, respectively. Delayed Pain Ratings did not show evidence of heritability, and therefore was not examined in the analyses of our exploratory aim.

3.5 Quasi-Causal Models for the Relationship between Pain Catastrophizing and CPT Outcomes

Given statistically significant phenotypic associations between pain catastrophizing and CPT outcomes as well as evidence of heritability for pain catastrophizing, CPT Immersion Tolerance, and CPT Pain Tolerance, we tested our exploratory aim—that is, whether these phenotypic associations were direct or, alternatively, partially attributable to shared genetics and/or environmental influence. Accordingly, we used the quasi-causal twin models described above. In these models, $c\text{-reg}$ (i.e., the contribution of PCS common environment to CPT phenotypic variance) was set to zero because PCS score, CPT Immersion Tolerance, and CPT Pain Tolerance had no common environmental (C) variance and were therefore modeled as a function of additive genetics (A) and unique environment (E) only. Table 5 shows the phenotypic and $a\text{-reg}$ (i.e., the contribution of PCS additive genetics to CPT phenotypic variance) for CPT Immersion Tolerance and CPT Pain Tolerance. For CPT Immersion Tolerance, the phenotypic regression was no longer statistically significant (model RMSEA = .04). *This suggests the possibility of genetic confounding* (i.e., the phenotypic effect was no longer significant when controlling for shared genetics) or perhaps insufficient power to achieve statistical significance while controlling for genetics. The latter seems more likely given that the magnitude of the regression coefficient was similar to that seen without controlling for genetics (phenotypic association without controlling for genetics = -1.01 , 95% CI = $-1.98 - -0.04$; phenotypic association while controlling for genetics = -1.16 , 95% CI = $-2.60 - 0.28$) and the $a\text{-reg}$ was *ns*. For CPT Pain Tolerance, the phenotypic regression coefficient remained significant ($p = .029$; model RMSEA = .03). *This suggests a direct relationship between pain catastrophizing and CPT Pain Tolerance.*

4. Discussion

Twin studies are uniquely suited to address questions regarding the origins of and relationships between complex behavioral phenomena. We used a sample of MZ and DZ twins to examine the heritability of pain catastrophizing and the potential confounding of the observed relationship between pain catastrophizing and experimental pain responses by shared genetics and common environmental exposure. We found that pain catastrophizing was significantly associated with CPT outcomes. More importantly, we found that pain catastrophizing showed significant evidence of heritability. Finally, exploratory analyses

found that associations between PCS and CPT outcomes may not be significantly attributable to shared genetics or environmental exposure.

To our knowledge, the current study is the first effort to examine the heritability of pain catastrophizing -- a central predictor of adverse acute and chronic pain outcomes [1, 2, 5, 6]. The observed heritability estimate for pain catastrophizing (37%) appears in line with heritability attributed to non-pain-specific coping constructs; for example, twin studies of stress coping outside the context of pain have found that genetic factors account for 20% to 50% of individual difference variance [29]. Previously examined categories of coping have broadly included social support seeking, problem-focused coping, emotion-focused coping, and avoidant coping/distraction approaches [30–33]. Studies also have identified a genetic contribution to traits associated with catastrophizing and pain response, including anxiety sensitivity (e.g., 45%) [34] and neuroticism (e.g., 50%) [35]. To further appreciate the magnitude of heritability identified in the current analysis, it is worth noting that the heritability psychological constructs (e.g., depression) as well as physical symptoms (e.g., somatic complaints) that may be associated with pain outcomes are around 40% (for review, see [35]).

Our findings suggest that similar to other individual-difference constructs, there is a significant genetic basis for pain catastrophizing. However, we also found that *unique environmental factors* contributed significantly to the variance in pain catastrophizing. These results are consistent with previous findings that unique environmental factors contribute an additional 50% to 80% to the variance in coping response [30–33]. Research on unique environmental contributors to pain catastrophizing is sparse, although some clues are offered by studies linking pain catastrophizing in adults with a history of traumatic experiences [36]. A role for unique environmental factors is potentially consistent with the social learning perspective on pain catastrophizing [6, 11], highlighting the importance of the learning environment in the development of one's understanding and processing of pain. Studies indicate that individuals with negative orientations toward pain, such as catastrophizing and pain-related fear, selectively attend to pain information in the environment [37–40] (but see [41]) and appraise observed pain experiences as being more painful [42]. Further, those with high fear/catastrophizing appear more sensitive to evidence confirming rather than disconfirming negative pain schemas [43, 44]. Such biased learning is hypothesized to reinforce existing negative pain schemas and associated patterns of pain behavior [45, 46]. Given that our findings point to the impact of unique rather than shared environmental influences, future studies should examine a potential *interaction* between individuals' heritable psychological orientation toward pain and pain-relevant environmental exposures.

Although not a central aim of our study, our findings also contribute to the small but growing literature on the heritability of experimental pain responses. To date, surprisingly few studies have examined the heritability of responses to experimental pain stimuli. The substantial genetic and environmental contributions to the tolerance indices from the CPT task complement previous evidence of heritability in individuals' response to a variety of experimental pain stimuli [47–49]. However, our results are difficult to compare with previous findings as methodology, pain modality, and collected measures have varied

greatly across studies, with most studies examining self-report rather than behavioral indices. Consistent with our findings, the only study that reported heritability estimates for a behavioral measure of CPT response [50] found that 49% of the variance in CPT immersion tolerance was attributable to genetic factors in a twin sample.

The current study is also the first to examine the association between pain catastrophizing and response to experimental pain with respect to potential shared genetic or environmental variance. We found that the relationship between pain catastrophizing and experimental pain responses (specifically CPT Immersion Tolerance and Pain Tolerance) was not significantly determined by shared genetics and common environmental exposure. Stated another way, the heritability of pain catastrophizing did not appear related to the heritability of responses to the experimental pain task. Although needing replication, this finding is potentially informative regarding the mechanisms underlying the link between pain catastrophizing and one's experience of and response to painful stimuli. If, as our exploratory findings suggest, shared genetic factors do not account for the phenotypic association of pain catastrophizing and experimental pain response, then it is feasible that the association between pain catastrophizing and pain responses could potentially be a direct one. A number of clinical and experimental studies support the antecedent role of catastrophizing in pain experience [51–53], however, our current findings do not allow us to determine whether high pain catastrophizing predisposes one to lowered pain tolerance or whether a genetic predisposition toward lower pain tolerance leads to higher pain catastrophizing over time that may then amplify and maintain the behavioral response to pain. Nonetheless, our finding of a potentially direct association combined with the previous research that has identified pain catastrophizing as a significant risk factor for the development of adverse pain responses [1–4] suggests that this area is worthy of further investigation. Future prospective studies can further clarify the mechanisms linking pain catastrophizing and pain response, shed light on the direction of this association, and examine potential mediators (e.g., attention, appraisal, or behavioral processes) and moderators (e.g., age, gender) of the relationship.

Interestingly, we found that pain catastrophizing showed a greater association with CPT Immersion Tolerance and Pain Tolerance rather than self-reported pain ratings (i.e., Threshold Pain Rating and Immersion Tolerance Pain Rating) from the CPT. This is surprising given that findings linking elevated catastrophizing with higher pain report are more consistent than those linking catastrophizing with pain threshold or tolerance [51]. However, our results are in line with findings linking pain catastrophizing and associated constructs with greater avoidance of painful physical activity [54, 55]. While not directly analogous to pain behavior, decreased tolerance of painful activity can serve a communicative function to the social environment [51]. Indeed, studies have linked catastrophizing with heightened display of pain behavior [54, 56]. Interpersonally-oriented pain expression may further contribute to the unique learning environment that informs individuals' beliefs about pain, potentially driving the interaction of heritable predispositions and environmental input.

Taken together, our findings suggest that there are both genetic and unique environmental influences on pain catastrophizing and experimental pain outcomes. Clearly, identifying

modifiable environmental factors such as excessive exposure to pain stimuli and examining the genetic, environmental, social, and cultural mechanisms that contribute to pain catastrophizing can lead to more effective prevention and treatment strategies. Our results support the utility of targeting pain catastrophizing in intervention and some studies have noted that addressing pain catastrophizing directly can result in better adjustment to acute and chronic pain [5, 57, 58]. Further, comprehensive assessment of pain catastrophizing that addresses both genetic or family history as well as one's unique learning history can help to refine these interventions for better outcomes.

This study has several limitations. First, the study examined experimental pain within a laboratory setting with a relatively healthy community sample and thus does not represent clinical pain experience. However, there is evidence that responses to experimental pain may be predictive of clinical pain responses [59] and a recent study suggested that cold pressor pain may have particular validity in understanding genetic contributions to clinical pain phenomena [50]. It is also possible that we would have found larger heritability estimates in a clinical sample with greater variability in pain catastrophizing. Future research is encouraged to examine the relative contribution of genetic factors to catastrophizing and pain outcomes in clinical samples. Second, due to power limitations, we did not examine the influence of participant sex in the heritability of pain catastrophizing; given evidence of sex differences in catastrophizing, pain responses, and pain-relevant genetic factors [51, 60, 61], this is an important issue to examine in future studies. Third, the study sample was relatively young (average age = 29 years), so we were not able to examine potential changes in genetic influence by age [29]. Given the robust predictive value of pain catastrophizing in both adult and child samples, it may be valuable to examine the genetic influences on pain catastrophizing across the lifespan. Finally, given the value but relative paucity of existing literature, future research is encouraged to examine genetic contribution to experimental pain responses.

In conclusion, the current study provides novel findings supporting the heritability of pain catastrophizing. Moreover, this is the first study to suggest that the observed association between pain catastrophizing and experimental pain response may be direct rather than owing to shared genetic or environmental influence. Pain catastrophizing represents a major psychological risk factor in pain adjustment and outcomes; therefore, continued efforts to elucidate its development and mechanisms remain a priority.

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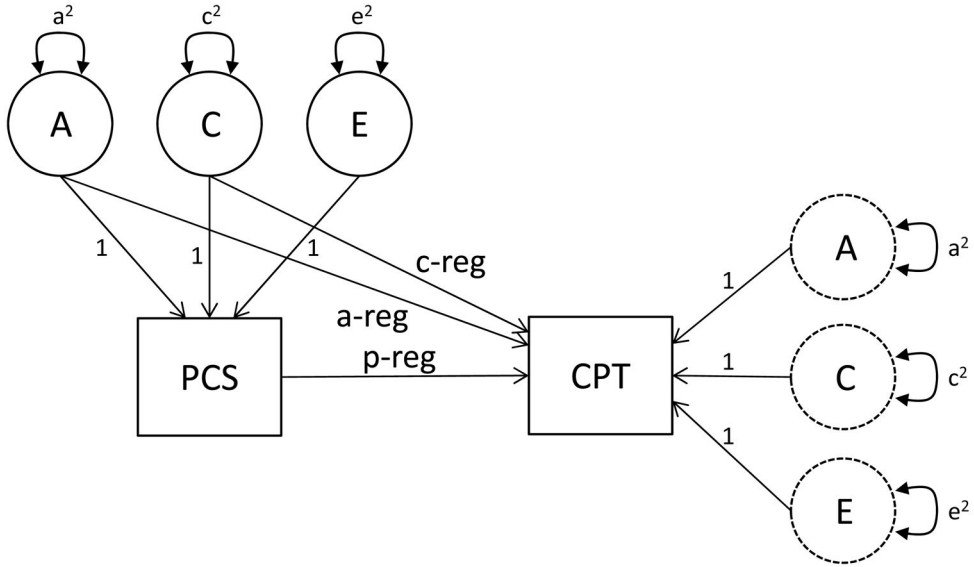


Figure 1. Simplified path diagram of the quasi-causal regression model.
Note: A = additive genetics; C = common environment; E = unique environment; PCS = pain catastrophizing scale; CPT = cold pressor test; p-reg = phenotypic regression; a-reg = contribution of PCS additive genetics to CPT phenotypic variance; c-reg = contribution of PCS common environment to CPT phenotypic variance. C variance (c^2) for PCS and c-reg were set to zero in this model because there was no C variance in PCS. The path diagram is simplified in that it includes only one member of the twin pair. The full figure would have a second complete version of the above Figure with within-pair correlations between the A and C components for both PCS and CPT.

Table 1

Sample Characteristics and Cold Pressor Task (CPT) Outcomes

	Full Sample (n = 400)	DZ (n = 194)	MZ (n = 206)	p
Female, %	53.0	54.6	51.5	ns
Age, Years (SD)	28.8 (12.3)	30.7 (13.4)	27.0 (10.8)	.031
Race, %				
White	80.0	81.4	78.6	
Black	5.8	6.7	4.9	
Asian	7.0	5.7	8.3	
NA/PI/Other	6.2	6.2	8.2	
PCS, Mean (SD)	8.9 (7.9)	8.3 (7.4)	9.5 (8.3)	ns
CPT Indices, Mean (SD)				
Pain Threshold (seconds)	16.7 (26.2)	16.1 (23.7)	17.3 (28.4)	ns
Immersion Tolerance (seconds)	75.1 (92.3)	75.2 (93.4)	75.0 (91.5)	ns
Pain Tolerance (seconds)	58.3 (87.9)	59.1 (90.0)	57.6 (86.0)	ns
Threshold Pain Rating (VAS)	35.5 (19.4)	36.1 (20.6)	34.9 (18.2)	ns
Immersion Tolerance Pain Rating (VAS)	65.2 (19.7)	66.0 (19.4)	64.4 (20.1)	ns
Delayed Pain Rating (VAS)	6.9 (9.9)	7.5 (11.3)	6.3 (8.2)	ns

Note: DZ = Dizygotic twin pairs; MZ = Monozygotic twin pairs; Delayed Pain Rating = 5-min post hand withdrawal; pain ratings were made on a 0–100 mm visual analog scale (VAS).

Table 2

GEE Bivariate Associations between Pain Catastrophizing and Cold Pressor Task (CPT) Outcomes

	Estimate	95% CI	<i>p</i>
Pain Threshold (seconds)	-0.083	-0.365 – 0.198	ns
Immersion Tolerance (seconds)	-1.006	-1.976 – -0.036	.042
Pain Tolerance (seconds)	-1.090	-2.103 – -0.076	.035
Threshold Pain Rating	0.102	-0.134 – 0.338	ns
Immersion Tolerance Pain Rating	-0.065	-0.294 – 0.164	ns
Delayed Pain Rating	0.234	0.080 – 0.388	.003

Note: GEE = Generalized estimating equations; CI = confidence interval

Table 3

Correlations amongst Cold Pressor Task (CPT) Outcomes

Variable	1	2	3	4	5
1. Pain Threshold (seconds)					
2. Immersion Tolerance (seconds)	.60**				
3. Pain Tolerance (seconds)	.31**	.89**			
4. Threshold Pain Rating (VAS)	-.08	-.29**	-.31**		
5. Immersion Tolerance Pain Rating (VAS)	-.16**	-.20**	-.14**	.59**	
6. Delayed Pain Rating (VAS)	-.06	.02	.06	.24**	.19**

** $p < .01$

Table 4

Within-pair Correlations and Variance Components Estimates

Scale or Variable	Variance Components			
	rDZ	rMZ	h ²	e ²
PCS	.04	.45*	37%	63%
CPT Immersion Tolerance (seconds)	.22*	.56*	55%	45%
CPT Pain Tolerance (seconds)	.21*	.53*	52%	48%
CPT Delayed Pain Rating (pain)	-.03	.04	-	100%

Note:

* $p < .05$; h² = heritability; e² = unique environment

Table 5

Quasi-Causal Models of Pain Catastrophizing and CPT

Variable	Phenotypic Regression	95% CI	<i>p</i>	A Regression	95% CI	<i>p</i>
CPT Immersion Tolerance	-1.55	-2.95 – -0.15	.029	1.51	-2.91 – 5.93	ns
CPT Pain Tolerance	-1.16	-2.60 – 0.28	ns	0.21	-4.35 – 4.77	ns

Note: CI = Confidence Interval