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Clinical phenotyping of youth with new-onset musculoskeletal pain: A controlled cohort study

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Abstract

Objectives—The course of pediatric musculoskeletal pain from acute to chronic has not been well described and there is limited understanding of how to identify individuals with new onset pain who may be predisposed to developing persisting symptoms. Thus, the purpose of this study was to describe the clinical phonotype of treatment-seeking youth with new onset musculoskeletal pain compared to youth with and without chronic pain. Further, we tested predictors of pain-related disability and pain sensitivity in the new onset pain sample.

Methods—Participants were 191 youth ages 10–17 years representing three cohorts (new onset musculoskeletal pain, chronic musculoskeletal pain, and a comparison group without chronic pain). Youth completed questionnaire measures of pain characteristics, psychological functioning, sleep and pain-related disability. They also attended a laboratory visit to complete an experimental pain assessment using heat and cold stimuli to assess pain sensitivity and conditioned pain modulation.

Results—Findings revealed youth with new onset musculoskeletal pain had a distinct clinical phenotype where symptoms of pain and disability were in the mid-range between those of youth with diagnosed chronic musculoskeletal pain and youth in the community without chronic pain. Linear regressions within the new onset pain sample demonstrated poorer sleep quality and higher pain fear predicted greater pain-related disability, and pain catastrophizing predicted cold pressor sensitivity.

Discussion—Clinical phenotyping of youth with new onset musculoskeletal pain highlights factors relevant to the pain experience. Future research can examine the roles of these variables in predicting longitudinal risk for chronic pain and disability.

Keywords

acute pain; chronic pain; musculoskeletal; pediatric

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Pain accounts for 22 – 39% of primary care appointments during childhood and adolescence [1], with musculoskeletal pain alone accounting for 11% of medical visits in youth aged 11–14 years [2]. Prevalence of musculoskeletal pain complaints increases with pubertal development, placing adolescents at highest risk [3]. Knee, spine, and foot pain are the most common musculoskeletal pain complaints in youth [4, 5], stemming from both traumatic (falls, sprains) and non-traumatic (poor posture, overuse, immobilization) etiologies. When musculoskeletal pain persists over time, youth experience a range of negative consequences including impact on their physical, emotional, and social functioning, as well as on overall quality of life [6, 7].

The economic costs of musculoskeletal pain are high and are primarily due to a small minority of individuals who go on to develop chronic pain. Resultant health care utilization, work limitations, disability, and disability compensation are estimated at $635 billion annually in the United States [8, 9]. Within pediatric populations exclusively, expenditures for moderate to severe pain are estimated at $19.5 billion [10]. Increasingly research has focused on the identification of potentially modifiable risk factors to prevent the transition from acute to chronic pain. A first step is documenting the course of musculoskeletal pain following onset of a new pain problem. As of yet there is an incomplete understanding of how to identify youth with new onset musculoskeletal pain who are predisposed to developing chronic and ongoing symptoms.

Longitudinal epidemiologic studies have identified several risk factors for musculoskeletal pain persistence or recurrence including: female sex, older age, high pain-related disability, multiple site pains, psychological disturbance, short sleep duration, and somatic symptoms [11–14]. However, it is unknown whether similar clinical or psychological factors might be used to identify youth at risk for poor recovery from new onset musculoskeletal pain. In particular the clinical phenotypes of youth who seek treatment for new onset musculoskeletal pain have not been characterized. If clinicians were able to identify youth at high risk then early intervention could be implemented to try to prevent development of chronic disabling musculoskeletal pain. At present, available pediatric data on risk factors for musculoskeletal pain are predominantly limited to school-based surveys of community samples.

A pivotal mechanism underlying chronic musculoskeletal pain is sensitization of central pain pathways. Sustained acute pain can amplify responses to noxious inputs and impair function of inhibitory and facilitatory pain pathways [15, 16]. In adults, altered central pain processing has been shown to be a risk factor for chronic pain post-surgery [17] and for the development of new chronic pain problems over time [18]. In pediatric samples, only a few studies have measured alterations in pain processing to compare youth with and without chronic pain (e.g., [19]). To date, no research has examined altered central pain processing as a risk factor for development of chronic pain in children, and therefore studies are needed to determine the relevance for predicting risk for pain persistence and chronicity in youth.

Additionally, pain-specific psychological factors, including fear of pain and pain catastrophizing, may also impact the persistence of pain in youth. The fear-avoidance model proposes that pain catastrophizing and pain-related fear contribute to pain persistence by

promoting and maintaining behavioral avoidance and activity limitations [20, 21]. Both fear of pain and pain catastrophizing have been found to predict pain intensity, pain-related disability and pain persistence in community samples and youth with existing chronic pain [22–24]. Assessing these pain cognitions in youth with new onset pain may inform our understanding of modifiable risk factors.

Therefore, we designed a longitudinal study in order to identify risk factors for predicting the persistence of musculoskeletal pain among youth with new-onset (< 1 month duration) musculoskeletal pain presenting for evaluation in emergency medicine or an orthopedic clinic. We conducted clinical phenotyping at baseline and follow-up assessment 4 months later which included comprehensive measurement of pain characteristics, psychological functioning, pain-related disability, sleep quality, and quantitative sensory testing. This manuscript reports on findings from the baseline assessment only; follow-up data collection is still in progress. Specific aims were to: 1) compare youth with new onset musculoskeletal pain to both a clinical sample of youth with diagnosed chronic musculoskeletal pain and to youth in the community without chronic pain in order to identify similarities and differences in clinical phenotypes at baseline, and 2) to determine within the new onset pain sample factors that are associated with pain-related disability and pain sensitivity, which may predict increased risk for chronic pain.

Method

This study was conducted at an academic medical center in the northwestern United States. All study procedures were approved by the Institutional Review Board, and all participants provided consent or assent prior to participating. Child and adolescent participants were ages 10–17 years and enrolled in an ongoing longitudinal study examining psychophysical factors that were associated with the transition from acute to chronic musculoskeletal pain in youth. The sample included three cohorts: 69 children with new-onset musculoskeletal pain presenting to an orthopedic clinic or emergency medicine (new onset pain sample), 60 children with chronic musculoskeletal pain undergoing an initial evaluation in a specialty pediatric pain clinic, and 62 youth without chronic pain recruited from community advertisements and well-child visits to primary care practices.

Children in the new onset pain sample were treatment-seeking youth presenting to the emergency department (n=31) or orthopedic clinic (n=38) for evaluation of a new musculoskeletal pain complaint (e.g., limb, back or neck pain). Inclusion criteria included presence of pain for less than one month at time of enrollment. Participants were excluded if serious pathology (e.g., infection, disease process) was associated with the source of the pain complaint or participants had a surgical procedure (including reductions) at the pain site. Youth were also excluded if they had another current chronic pain condition (e.g., chronic headaches or recurrent abdominal pain) or a history of chronic pain or surgery at the site of the acute pain complaint.

Inclusion criteria for youth with chronic musculoskeletal pain were: a diagnosis of chronic musculoskeletal pain in the limb(s), back or neck based on evaluation in an interdisciplinary pain clinic, and pain present for 3 months or greater occurring at least weekly, and

associated with functional impairment. Youth with chronic pain were excluded if their musculoskeletal pain was associated with a serious pathology (e.g., cancer, inflammatory arthritis).

Inclusion criteria for youth without chronic pain were no history of or current complaint of chronic or recurrent pain.

Across all groups, youth and their parents were required to be able to independently complete written questionnaires and be proficient in English to participate.

Procedures

Potential participants with acute and chronic musculoskeletal pain were identified by clinical staff or from clinic schedules and invited to participate in the research study. Families were then contacted via phone to undergo additional screening for inclusion/exclusion criteria. Interested families of youth without chronic pain responded to flyers in the community or pediatric practices during well child visits and called research personnel for information about the study.

Participating families provided written assent/consent before undergoing any study procedures. The procedures included an in-person laboratory visit at baseline. During their laboratory visits, children underwent experimental pain tasks to assess pain sensitivity and completed questionnaire measures of pain characteristics, sleep, and psychosocial functioning. All procedures were administered by trained research assistants and scripted instructions were read to the child or adolescent to insure uniform experimental conditions. The pain sensitivity assessment took approximately 20 minutes, with total assessment procedures (including consent and measure administration) estimated at one hour.

Questionnaire Measures

Demographics—Parents reported on their child's age, sex, and race.

Body Mass Index (BMI)—Study staff collected children's height and weight measurements during their laboratory visits. Height and weight information was entered into the Center for Disease Control's online calculator (https://nccd.cdc.gov/dnpabmi/calculator.aspx) to calculate BMI corrected for age and sex.

Pain—Pain was assessed using youth report of pain intensity, pain frequency, and pain bother. Specifically youth were asked to report on their "usual pain intensity" over the past 7 days using a Numerical Rating Scale (11 point NRS 0–10). Reports of the frequency of pain symptoms were also assessed, with youth using a 6 point ordinal scale (0–5; 0 = "less than once/month" to 5 = "daily") to describe how often pain occurred over the last 7 days. Pain bother was assessed with the question "how much do aches or pains bother or upset you?" with five response options (0 = "not at all" to 4 = "very much"). These pain assessment items have been used in previous studies of youth with and without chronic pain [25, 26].

Depressive Symptoms—Adolescents completed the 20-item Center for Epidemiological Studies Depression Scale (CES-D) to assess depressive symptoms. Item responses on the

CES-D range from 0 (Rarely or none of the time; less than 1 day) to 3 (Most or all of the time; 5–7 days) and are summed to create a total score ranging from 0–60, with higher scores indicating greater depressive symptoms. The CES-D is widely used to assess depressive symptoms in children and adolescents, and has demonstrated acceptable 1-week test-retest reliability [27]. Validity of the CES-D is supported by documented relationships with other measures of internalizing symptoms [27]. A CES-D score of 16 or greater indicates clinically significant depressive symptoms [27].

Pain-Related Disability—The Child Activity Limitations Interview (CALI-21) was used to assess pain-related disability in children and adolescents [28]). This 21-item measure asks participants to report on ability to participate in 21 activities over the previous 4 weeks, using 5 response options ranging from 0 ‘not difficult’ to 4 ‘extremely difficult’. A total score is calculated by summing ratings for all 21 items (range from 0 – 84), with higher scores indicating greater functional disability due to pain. The CALI-21 child and parent versions have demonstrated reliability and validity in assessing pain-related disability in school aged children and adolescents [28].

Sleep—The 28 item Adolescent Sleep-Wake Scale (ASWS) was used to assess adolescent perceptions of sleep quality [29]. Adolescents reported on their sleep during the previous month along a 6-point scale (range from 1=always to 6=never) with higher scores indicating better sleep quality. The ASWS measures five behavioral dimensions of sleep (going to bed, falling asleep, maintaining sleep, reinitiating sleep, returning to wakefulness). A total score on the ASWS was used in analyses. The ASWS is a valid and reliable assessment tool that has been used extensively in both pain and non-pain populations [30, 31].

Fear of Pain—Adolescents reported fear and avoidance related to pain using the Fear of Pain Questionnaire (FOPQ-C) [32]. The 24 items on the scale are rated on a 5-point scale ranging from 0 (strongly disagree) to 4 (strongly agree) and items are summed for a total score, with higher scores indicating more pain-related fear. In the validation study the FOPQ-C demonstrated excellent reliability and construct validity and the measure has subsequently been used to asses pain fear in diverse pain samples [33, 34].

Trait Pain Catastrophizing—The Pain Catastrophizing Scale for Children (PCS-C) was used to assess catastrophizing about pain symptoms in children and adolescents [35]. The measure prompts participants to reflect on past painful experiences and to indicate the degree that they experienced ruminating, magnifying, or helpless thoughts or feelings related to each question. Response options are on a 5-point scale (0–4) ranging from 0 (not at all) to 4 (extremely). This scale shows good internal consistency and reliability and has been validated for use with 8 to 16 year old children [35]. Recently an updated scoring system was published which uses an 11 item total score (eliminating items 7 & 8) for analyses and presents three new clinical reference points (low 0–14; moderate 15– 25; and high 26 and greater catastrophizing symptoms [36]. The 11 item scoring system and clinical cut-points were used in the analyses.

State Pain Catastrophizing—State pain catastrophizing was assessed during the laboratory task using the following four questions: 1) “how unpleasant did you find the

task?, 2) to what extent did you keep thinking about how much pain you experienced during the task?, 3) to what extent did you think that, because of the pain, something serious might happen during the task?, and 4) to what extent did you think, because of the pain, you would not be able to endure the hot and cold task?" Response options ranged from 0 "not at all" to 10 "a lot" and were summed for a total state pain catastrophizing score. These items have previously been used in other laboratory pain studies to assess trait pain catastrophizing [37].

Pain Sensitivity—Adolescents participated in a hot and cold thermal task to assess pain sensitivity and conditioned pain modulation. Procedures are a modification of methods used in an adult study examining risk for post-surgical pain [38] and in a pediatric study of children with IBS [19]. In this laboratory task, children underwent a series of heat sensations applied to their dominant inner forearm, first alone, and then in conjunction with the child's non-dominant hand in a cold water bath. Heat stimuli were produced by a Thermal Sensory Analyzer (Medoc) with a 30mm × 30mm surface stimulator. Baseline heat temperature started at 32.0°C with an increasing temperature rate of 1.5°C and a cooling rate of 8°C/s. For safety, a maximum temperature was set at 52°C. After each heat sensation the thermode was moved to an adjacent location on the child's forearm to prevent sensitization. Cold stimulus was produced with an 8°C circulating water bath (cold pressor).

Test stimulus: First, youth underwent a brief training phase (a series of 2 heat sensations) to familiarize them with the heat stimuli device, instructions and perceived sensations. Participants were then administered a series of 4 heat sensations and were instructed to push a button on a controller "when the heat becomes painful" (baseline heat pain threshold; B-HPT). Instructions explicitly stated that assessment was for a pain threshold, not how much heat they could tolerate.

Conditioning Stimulus: Next, youth were instructed to immerse their non-dominant hand (just above wrist) in the 8°C circulating water bath for 20 seconds. With their non-dominant hand in cold water, youth underwent a series of 3 heat pain sensations. Once again, they were instructed to push a button on a controller "when the heat becomes painful" (conditioning heat pain threshold; C-HPT). To assess cold pain sensitivity, participants were asked to rate pain intensity (NRS 0–10) of the cold pressor immediately following this task.

Conditioned Pain Modulation: A conditioned pain modulation (CPM) index score was calculated using the ratio of the C-HPT with the conditioning stimulus (cold pressor) to the B-HPT multiplied by 100. A greater index score indicates a larger CPM effect. This method of calculation of CPM has been used in other laboratory tasks examining pain sensitivity in clinical pain samples [39].

Statistical Analyses

Data were analyzed using SPSS v.20. Summary statistics were used to describe characteristics of the sample, and are reported separately for each group (Table 1). Means and standard deviations were used for continuous data, and categorical items were described using frequency statistics. We present a detailed description of the new onset pain cohort since this population has not previously been characterized. To address our first aim

examining similarities and differences in clinical phenotypes between youth with new onset musculoskeletal pain, youth with chronic musculoskeletal pain and youth without chronic pain, multivariate analysis of covariance (MANCOVAs) were conducted via the general linear model command in SPSS across the three domains of interest: pain and disability, pain sensitivity, and sleep/psychosocial functioning. Age, sex, BMI, and race (recoded Caucasian versus non-Caucasian) were included as covariates in all MANCOVAs to account for differences by study group.

To address the second aim to determine within the new onset pain sample the factors that predict pain risk (pain-related disability and pain sensitivity), three step-wise multiple linear regression models were conducted. The first model tested predictors of pain-related disability (CALI total score). The next two models tested predictors of pain sensitivity (both cold pressor pain and CPM index). Child sex, age, BMI, and race were controlled for in Step 1, usual pain intensity was entered in Step 2, and depressive symptoms, fear of pain, sleep quality, state pain catastrophizing, and trait pain catastrophizing were entered in Step 3 of these models.

Considerations for experimental pain data—A small number of youth (n=14) stopped the experimental pain tasks before completion because they reported it was too painful to continue (6 in the new onset pain cohort and 8 in the chronic pain cohort). Furthermore, three participants in the new onset pain cohort could not participate in the conditioning stimulus (cold pressor) due to having a non-removable cast on their non-dominant arm or hand. A priori we decided to use the mean of available data for each participant on the thermal sensitivity tasks to maximize data points for analysis. This provides a more conservative estimate of pain sensitivity than excluding all data for participants who did not complete the task.

Results

A total of 191 youth participated in this study (69 new onset pain, 62 chronic pain, and 60 without chronic pain). Demographic characteristics of the 3 cohorts are presented in Table 1. Groups were different on age, sex, BMI, and race. Specifically the chronic pain sample was older and comprised of more females than the other two cohorts. In addition, the new onset pain sample was comprised of more non-Caucasians, in particular children who identified as having more than one race than the other two cohorts. Youth with new onset pain also had higher BMI than healthy youth. Thus, these demographic variables were used as covariates in subsequent models.

Description of New Onset Musculoskeletal Pain Cohort

The new onset musculoskeletal pain cohort consisted of 69 youth recruited from either the emergency department (n=31) or orthopedics (n=38). The most common sites of musculoskeletal pain in this sample were leg/foot pain (43.5%) followed by back (13.0%), head (13.0%) and hand/arm pain (10.1%). The majority of youth reported experiencing 1 or 2 pain locations (44.9% and 34.8% respectively), with a mean of 1.78 pain sites (SD=1.26). 29.4% of youth experienced a fracture as a reason for their pain. The most commonly reported etiology for their pain was sports (58.0%) followed by non-sports related accidents

(21.7%), unknown etiology (13.0%), and other reasons (5.8%). Youth with and without fractures differed on usual pain intensity over the last 7 days. While youth in both groups reported experiencing moderate to high levels of pain, pain intensity in the group who had experienced a fracture was lower (M=4.10, SD=1.80) than those without fractures (M=5.23, SD=2.11) t(66)=2.10, p=.04. Usual pain intensity was not different by referral source (emergency department versus orthopedics).

A portion of youth in the new onset pain group endorsed significant psychological symptoms using established measure cut-offs. Specifically, 33.3% had clinically significant depressive symptoms (CES-D score ≥16) and 24.6% had moderate to high levels of catastrophizing about pain (PCS-C scores ≥ 15). Youth with and without fractures did not differ on depressive symptoms, pain catastrophizing, or fear of pain.

Similarities and Differences in Clinical Phenotypes by Cohort

To account for group differences on age, sex, BMI, and race, these four variables were used as covariates in multivariate models. Three separate MANCOVAs were used to determine group differences on 1) pain characteristics and pain-related disability, 2) self-reported psychosocial functioning and sleep, and 3) experimental pain responses.

In the first analysis evaluating group differences on pain characteristics and pain-related disability, the multivariate model was significant for group, Wilk's Λ =.41, F(8,346) = 24.45, p<.001, η^2 = .36. Follow-up univariate tests revealed differences on pain frequency, pain intensity, pain bother, and activity limitations (see Table 2). Specifically, youth with new onset pain reported significantly higher pain (frequency, intensity and bother) and greater disability than healthy youth, but had less pain (frequency, intensity and bother) and disability than the chronic pain sample. Examination of covariates revealed child age was significantly associated with activity limitations with older youth reporting greater pain-related disability.

In the second analysis evaluating group differences on self-reported sleep and psychological functioning (depressive symptoms, pain catastrophizing, fear of pain, sleep quality), the multivariate model was significant for group, Wilk's Λ =.71, F(10,300) = 5.57, p<.001, η^2 = .16. Follow-up univariate tests revealed youth with new onset pain were similar to healthy youth on psychosocial and sleep variables (see Table 2). However, youth with new onset pain reported significantly better sleep quality, lower depressive symptoms, pain catastrophizing (trait only), and pain fear compared to those with chronic pain. Examination of covariates revealed child age was significantly associated with depressive symptoms and child sex was significantly associated with fear of pain, with older youth reporting higher depressive symptoms (p<.001) and females reporting higher pain-related fear (p=.005).

In the third analysis evaluating group differences on experimental pain responses, the multivariate model was significant for group, Wilk's Λ =.85, F(8,332) = 3.51, p = .001, η^2 = .08 (see Table 2). Follow-up univariate tests revealed youth with new onset pain were similar to healthy youth on heat pain tolerance and cold pressor ratings but had significantly higher heat pain thresholds (both at baseline and during the assessment phase) and lower cold pressor pain intensity than youth with chronic pain. Youth with new onset pain did not

differ from the cohorts with or without chronic pain on the CPM Index. Examination of covariates revealed child age was significantly associated with heat pain threshold at baseline and during the assessment phase with older youth having higher heat pain thresholds (p's <.002). Child sex was associated with cold pressor pain intensity, with females reporting higher cold pressor pain ratings (p=.02).

Predicting pain risk in the new onset pain sample

To examine predictors of pain-related disability (CALI sum score) and pain sensitivity (cold pressor NRS and CPM Index), three separate stepwise linear regressions were conducted. Depression, fear of pain, sleep quality, and pain catastrophizing (state and trait) were entered as predictors. All stepwise models controlled for age, sex, BMI, and child race (recoded as Caucasian or non-Caucasian) (Step 1) and usual pain intensity (Step 2).

Results of the regression analysis predicting total CALI score in the new onset pain sample are presented in Table 3. Results revealed poorer sleep quality (B=−6.58, 95% CI.−12.61 – −.56, p=.03) and greater fear of pain (B=.35, 95% CI .09–.61, p=.01) predicted higher pain-related disability after controlling for age, sex, BMI, race and usual pain intensity. State catastrophizing, trait catastrophizing, and depressive symptoms did not predict pain-related disability.

Table 4 shows the findings of the regression analysis predicting cold pressor pain. Results revealed trait pain catastrophizing (B=−.11, 95% CI.-.21– −.01, p=.03) and state pain catastrophizing (B=.17, 95% CI .10–.24, p<.001) predicted cold pressor pain after controlling for age, sex, BMI, race and usual pain intensity. Interestingly, associations with the two catastrophizing variables were in different directions. While, as expected, *higher* state catastrophizing predicted higher ratings of pain during the cold pressor task, unexpectedly, *lower* trait catastrophizing predicted higher ratings of pain. Depression, sleep quality and fear of pain did not predict cold pressor pain ratings.

Controlling for age, sex, BMI, race and usual pain intensity, none of the hypothesized variables predicted the CPM Index score in the new onset pain sample.

Discussion

Chronic pain has an enormous impact both at the individual and societal levels, making research that can identify potentially modifiable risk factors preventing the transition from acute to chronic musculoskeletal pain critical. This work is particularly important for children and adolescents, who are at risk for having chronic pain persist into adulthood. Identification of potential targets for early intervention and prevention has the potential to reduce chronic pain across the lifespan. Findings from the current study add to the limited body of research by comprehensively describing the clinical phenotype of a treatment seeking sample of youth with new onset musculoskeletal pain compared to youth with and without chronic pain. A distinct clinical phenotype was observed in children and adolescents with new onset pain problems, in which symptoms of pain and disability fell in the mid-range between those of youth with diagnosed chronic musculoskeletal pain and youth in the community without chronic pain.

Despite reporting high pain and pain-related disability, overall, youth with new onset pain problems were similar in terms of sleep quality, pain sensitivity, and psychological functioning (e.g., depressive symptoms, pain catastrophizing) to healthy youth. This was not unexpected given that by definition these youth had new pain problems and the cycle of chronic pain, avoidance, and disability that is thought to drive negative emotionality in children and adolescents with chronic pain may not be established. That said, the results from this study show variability on psychological variables (e.g., a subsample of youth with new pain problems have clinically important depressive symptoms and moderate to high pain catastrophizing). Longitudinal data from this sample will help us understand whether high pain, disability and psychological symptomatology predict development of chronic musculoskeletal pain. Analysis of symptom clusters or subtypes will be particularly important as previous research in adolescents with chronic pain has demonstrated that dysfunctional versus adaptive symptom profiles differentially predict outcomes in these youth [40, 41].

Results also revealed that poorer sleep quality and greater fear of pain were associated with higher pain-related disability in children with new onset pain problems. This finding supports results from other studies demonstrating significant associations among disability and both pain-related fear and sleep in youth with chronic pain [42, 43]. Across new onset and more persisting pain, these factors appear to be relevant targets for assessment and/or intervention. Preventative interventions targeting these constructs could be routinely delivered to youth identified as having high symptomatology at time of pain evaluation. Longitudinal data will answer the question of whether factors such as pain-related fear and poor sleep quality predict pain persistence or more increasingly widespread pain, which may further support the need for early preventative intervention.

While previous research with children and adults with chronic pain has shown depressive symptoms predict concurrent disability and trajectories of pain over time [44, 45], contrary to expectations depressive symptoms were not associated with pain sensitivity or pain-related disability in the new onset pain sample. Seeking to explain these results it is possible that when pain has not yet become chronic general depressive symptoms may not relate as strongly to the experience of pain as other psychological factors including pain-related fear and pain catastrophizing. Follow-up data will reveal if the role of depressive symptoms changes with pain persistence, or if depression or sleep quality at baseline predicts symptom trajectories over time.

A central aim of this study was to assess pain sensitivity in youth with acute pain as part of clinical phenotyping. To our knowledge, no previous studies have conducted pain sensitivity testing in children and adolescents with new-onset musculoskeletal pain problems and compared these values with chronic pain and pain-free samples. Results of the current study revealed youth with new onset pain were similar to youth from the community in terms of heat pain thresholds and cold pressor pain ratings. Greater sensitivity (to heat and cold) in the chronic pain group supports some previous research however findings regarding differences in pain sensitivity among youth with chronic pain and healthy comparison samples are largely equivocal. Prior studies have found differences depending on the pain sensitivity task (e.g., thermal versus pressure), body location chosen as the testing site,

chronic pain location (e.g., abdominal pain) or presence of a chronic health condition (e.g., arthritis) [46]. Additional research should examine pain sensitivity in youth with new onset musculoskeletal pain using additional modalities such as pressure pain assessed via algometer, or pain sensitivity testing at multiple locations on the body to determine if findings differ by experimental methodology.

Contrary to expectations we did not see differences in conditioned pain modulation among youth with and without pain. Youth with new onset pain, chronic pain, and youth from the community had similar CPM index scores suggesting function of the endogenous pain inhibitory system was not different across groups. This finding is inconsistent with adult research that consistently shows differences in CPM in chronic pain and healthy samples (see review, [47]). In pediatric samples, some previous research supports differences in pain modulation among pain and comparison samples, for example, studies comparing heathy children to youth with IBS [19] and youth with early burn injuries [48]. While both of these studies showed poorer CPM in the clinical sample, effect sizes were small and other factors unique to the participants (e.g., age, sex) could have influenced the findings.

Age and sex have been shown to impact CPM in adult samples. In particular, males have a greater CPM effect than females, and older adults show less CPM suggesting the effect decreases with age [49]. While this sex effect has not been observed in children, research on CPM in a sample of healthy youth suggests age effects, with older children (12–17 years) showing greater CPM responses compared to younger (8–11 years) children [50]. It has been hypothesized that pain inhibitory mechanisms may develop throughout childhood, and become stronger during adolescence. In the current study it is possible we would have seen different CPM group effects if we used an exclusively older teenage sample. Including larger samples of youth of a broader age range is a direction for future research, which might help further elucidate the development of CPM across childhood and adolescence.

Unexpected, we found that state and trait pain catastrophizing differentially predicted cold pressor pain ratings in youth with new onset pain problems. As predicted, higher state catastrophizing (higher 0–10 NRS scores on 4 items assessing task unpleasantness, focus on pain during task, worry something serious might happen during the task, and concern of not being able to endure the hot and cold task) was associated with higher cold pressor ratings. In contrast, trait catastrophizing scores were in the opposite direction predicting lower ratings. The groups in our sample differed on trait catastrophizing but not state catastrophizing. This suggests that state and trait measures may have different patterns of relevance for chronic and acute pain experiences, and that trait catastrophizing may be less relevant to the acute pain experience. Moreover, the state catastrophizing questions include assessment of task unpleasantness, which might be closely related to cold pressor pain scores and thus contribute to the very high association between state catastrophizing and cold pressor NRS.

In terms of strengths, this study adds to the paucity of literature on treatment-seeking youth with new onset pain problems. The examination of a treatment-seeking sample of children and adolescents with new-onset musculoskeletal pain is unique, as no previous studies have described the clinical phenotype of this population using a combination of data on pain,

psychological factors, sleep, and laboratory pain sensitivity. Additionally the sample size of participants in each group was relatively large compared to prior studies comparing CPM in healthy youth versus youth with chronic pain which have had sample sizes of less than 30 participants in each group.

Limitations must also be emphasized. First, participants from all three groups were recruited from a single region of the United States and were predominantly Caucasian, limiting generalizability of the findings. An additional limitation is the diverse nature of the pain complaints in the new onset pain sample. The sample size was not large enough to systematically examine differences in clinical phenotypes by pain location, etiology of pain problem (e.g., sports injury versus accident) spatial distribution of pain problem (e.g., pain location, having one versus multiple pain complaint) or referral site (emergency department versus orthopedics). Moreover, this study did not assess additional clinical factors (e.g., joint hypermobility), history of injury, or expectations and beliefs about recovery. Future work might examine these factors and how they might contribute to pain presentation and/or disability in the context of athletic vs other acute injuries. While our assessment plan emphasized child self-report measures it will be equally important in future studies to also collect data on relevant parent and family factors that are known to predict pain-related disability. Finally, the current study used a single CPM protocol. While a similar protocol has been used in other published studies of children and adults [17, 19], it is possible that findings would be different with other pain stimuli (e.g., pressure pain, hot water rather than cold pressor).

In terms of future directions, the next step is to evaluate the persistence of pain at the four month follow-up. We will test these baseline variables (sleep disturbances, fear of pain, pain catastrophizing) that emerged as concurrent predictors of pain-related disability and pain sensitivity as predictors of pain persistence at follow-up. We will also establish preliminary rates of persistence of musculoskeletal pain in youth. Identification of predictors of pain persistence and chronicity are critical for developing preventative programs that have the potential to change the trajectory of pain for youth.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Descriptive characteristics of the sample

Variable	New onset pain n=69	Chronic pain n=60	Healthy n=62	*p*
	M(SD)/N(%)	M(SD)/N(%)	M(SD)/N(%)	
Age in years	13.98 (1.75)	14.58 (2.22)	13.63 (2.05)	.03
Sex				.01
Female	43 (62.3)	51 (85.0)	41 (66.1)	
Male	26 (37.7)	9 (15.0)	21 (33.9)	
Body Mass Index	23.30 (5.04)	23.19 (7.21)	21.02 (4.47)	.04
Race				
Caucasian/White	41 (59.4)	46 (76.7)	50 (80.6)	.007
African American/Black	4 (5.8)	3 (5.0)	4 (6.5)	
Asian	1 (1.4)	4 (6.7)	5 (8.1)	
American Indian/Alaskan	0 (0.0)	0 (0.0)	1 (1.6)	
More than one race	17 (24.6)	4 (6.7)	2 (3.2)	
Not reported	6 (8.7)	3 (5.0)	0 (0.0)	
Most painful pain location				<.001
Back or Spine	9 (13.0)	17 (28.3)	4 (6.5)	
Leg or foot	30 (43.5)	16 (26.7)	16 (25.8)	
Hand/arm	7 (10.1)	6 (10.0)	4 (6.5)	
Shoulder	5 (7.2)	3 (5.0)	1 (1.6)	
Hip	3 (4.3)	4 (6.7)	2 (3.2)	
Neck	6 (8.7)	3 (5.0)	0 (0.0)	
Head	9 (13.0)	2 (3.3)	2 (3.2)	
Chest	0 (0.0)	0 (0.0)	1 (1.6)	
Abdomen	0 (0.0)	1 (1.7)	5 (8.1)	

Table 2

Descriptive statistics and MANCOVA results of pain and psychosocial functioning variables

Pain and disability *						
	New onset pain *M* (*SD*)	**Chronic pain *M* (*SD*)**	**Healthy *M* (*SD*)**	**F (2, 176)**	**p**	**η^2**
Pain Frequency	2.52 (1.26)	3.66 (.69)	1.10 (.72)	102.78	<.001 *a,b*	.54
Pain Intensity (0–10 NRS)	4.95 (2.07)	6.32 (1.65)	2.93 (1.78)	44.54	<.001 *a,b*	.34
Pain Bother	1.95 (.94)	2.56 (.84)	1.10 (.72)	42.39	<.001 *a,b*	.33
Pain-Related Disability	15.54 (11.63)	26.51 (14.31)	4.76 (5.82)	50.49	<.001 *a,b*	.37
Psychosocial functioning *						
	New onset pain *M* (*SD*)	Chronic pain *M* (*SD*)	Healthy *M* (*SD*)	F (2, 154)	p	η^2
Fear of Pain	22.22 (16.68)	42.73 (18.84)	17.83 (12.10)	27.79	<.001 *a*	.27
Depressive Symptoms	14.24 (12.03)	23.44 (13.91)	13.09 (10.14)	7.86	<.001 *a*	.09
Sleep Quality	3.96 (.58)	3.54 (.78)	4.13 (.69)	8.29	<.001 *a*	.10
Pain Catastrophizing – Trait	9.78 (8.27)	18.65 (10.67)	7.62 (5.50)	20.83	.001 *a*	.21
Pain Catastrophizing - State	13.55 (7.51)	15.48 (8.71)	12.80 (6.85)	0.77	0.47	.01
Laboratory pain variables *						
	New onset pain *M* (*SD*)	Chronic pain *M* (*SD*)	Healthy *M* (*SD*)	F (2, 169)	p	η^2
Cold Pressor Pain (0–10 NRS)	5.98 (2.01)	6.91 (2.11)	5.60 (2.13)	4.1	.02 *a*	.05
Pain Threshold - Baseline	45.59 (3.93)	43.13 (4.23)	44.09 (4.38)	6.63	.002 *a*	.07
Pain Threshold - Assessment	45.83 (3.72)	43.51 (3.90)	45.03 (3.57)	7.44	.001 *a*	.08
CPM Index	100.78 (6.61)	101.19 (6.66)	102.51 (6.40)	1.1	0.34	.01

*Significant covariates: child age on pain-related disability (p=.007) and depressive symptoms (p=.001), baseline pain threshold (p = .002) and assessment pain threshold (p = .002); child sex on fear of pain (p = .005) and cold pressor pain (p = .02)

[a] chronic pain group significantly different from new onset pain and healthy groups

[b] new onset pain group significantly different from healthy group

Table 3

Summary of hierarchical linear regression analyses predicting pain-related disability (CALI total score) within the new onset pain sample

Variable	Step 1			Step 2			Step 3		
	B	***SE* B**	**β**	**B**	***SE* B**	**β**	**B**	***SE* B**	**β**
Sex	−2.16	3.18	−.09	−2.61	3.18	−.11	−5.04	2.72	−.22
Age	1.12	.95	.16	1.26	.95	.18	.99	.82	.14
Ethnicity	−4.17	3.27	−.17	−4.85	3.29	−.20	−2.23	2.95	−.09
Body Mass Index	−.403	.31	−.18	−.48	.31	−.22	−.44	.26	−.19
Pain Intensity				1.06	.81	.18	.81	.76	.14
Depression							.09	.14	.09
Fear of Pain							.35	.13	.51**
Sleep Quality							−6.58	2.99	−.34*
Trait Catastrophizing							−.17	.27	−.12
State Catastrophizing							−.27	.19	−.18
R^2 Δ		.08			.03			.35	
F for R^2		1.11			1.70			5.84***	

*p<.05,

**p<.01,

***p<.001

Table 4

Summary of hierarchical linear regression analyses predicting cold pressor pain within the new onset pain sample

Variable	Step 1			Step 2			Step 3		
	B	***SE* B**	**β**	**B**	***SE* B**	**β**	**B**	***SE* B**	**β**
Sex	.60	.57	.15	.55	.59	.14	.22	.49	.06
Age	−.17	.18	−.14	−.17	.18	−.14	−.24	.15	−.20
Ethnicity	.84	.58	.20	.78	.60	.19	.98	.53	.24
Body Mass Index	.01	.06	.03	.01	.06	.02	.02	.05	.05
Pain Intensity				.07	.16	.06	.06	.14	.06
Depression							.01	.02	.03
Fear of Pain							.03	.02	.23
Sleep Quality							−.24	.53	−.07
Trait Catastrophizing							−.11	.05	−.47*
State Catastrophizing							.17	.04	.59***
R^2 Δ		.08			.00			.39	
F for R^2		.98			.19			6.04***	

*p<.05,

***p<.001