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The role of puberty in experimental pain sensitivity in healthy adolescent girls

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Abstract

Introduction: Puberty is a critical developmental period during which changes in pain sensitivity are observed. Previous studies found that older and more mature adolescents have lower experimental pain sensitivity. However, it is unclear whether the differences in pain sensitivity are due to age or the pubertal maturation effect.

Objectives: This observational study examined the relationships between the pubertal maturation stage, age, and experimental pain sensitivity in healthy girls.

Methods: Healthy adolescent girls (n = 52, mean age 12.0 ± 1.4 years) completed the Pubertal Developmental Scale (PDS) to assess their pubertal stage. In addition, they completed a comprehensive quantitative sensory testing session, including pain thresholds, pain ratings to noxious stimuli, and pain modulation tests. Separate regression models were performed to assess the effect of pubertal maturation and age on experimental pain sensitivity as well as differences in experimental pain sensitivity between girls in different subjective self-perceived pubertal timing relative to peers.

Results: No relationships were found between the PDS score and experimental pain sensitivity; however, age was significantly related to cold pain tolerance ($P = 0.030$). In addition, to differentiate between puberty and age, experimental pain sensitivity was compared in a subsample of girls of the same age but at different pubertal stages, and no differences in experimental pain sensitivity were observed. No differences were also found when comparing girls who mature early, same, or late relative to their peers.

Conclusion: Puberty and age may have no effect on experimental pain sensitivity in healthy girls.

Keywords: Puberty, Age, Adolescents, Quantitative sensory testing

1. Introduction

Puberty is a critical developmental period that marks the transition from a nonreproductive to a reproductive state. Puberty can last several years, with physical changes typically starting to appear in girls around age 9 years and are completed around age 16 years.[24,38] Pubertal stages can be classified as prepuberty, early, mid, late, and postpuberty.[30] In addition to the physical changes in sexual characteristics, there are also significant biopsychosocial changes that happen during puberty and can affect nociceptive processing and pain, both chronic and experimental pain.[33]

Generally, as adolescents get older or mature, the sensitivity to experimental pain decreases.[3,4,23,29,42,44] However, many studies have focused on age differences rather than differences in pubertal maturation, and compared pain sensitivity among participants of different ages.[3–5,44] Because there is a large individual variability in puberty onset and the transition between the pubertal stages, adolescents of the same age may be at different pubertal stages.[11,18,46] Thus, the effect of puberty on pain is still unclear.

In addition to pubertal stages, pubertal maturation can be classified as relative pubertal timing, which is the maturation compared with peers (relatively early, same, or relatively late).[30] Early

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relative puberty is related to higher internalizing behaviors, including depressive symptoms,[16,22,45] which could affect pain sensitivity.

This study aimed to determine the role of puberty on experimental pain sensitivity in healthy girls. This study focused on girls since, during puberty, girls have an increase in chronic pain prevalence and greater experimental pain sensitivity compared with boys.[5,6,27,28,33] The associations between pubertal maturation scores and experiential pain measures were examined. Furthermore, in a subanalysis, girls of the same chronological age but different pubertal stages were compared, allowing disentangling between the effects of age and pubertal maturation. We hypothesized that more mature girls would have lower experimental pain sensitivity and more efficient pain modulation capabilities. In addition, exploratory analyses identified the effect of subjective self-perceived pubertal timing relative to peers on pain by comparing experimental pain sensitivity between adolescents who are in different puberal timing.

2. Methods

This study was approved by the Institutional Review Board of Washington University in St. Louis and was registered with ClinicalTrials.gov (NCT05145595). Data were collected between September 2022 and July 2024. Before participating in the study, all participants and their parents or guardians provided written informed consent and assent.

2.1. Study participants

Participants were recruited via flyers distributed using the research participant registry of Washington University School of Medicine, and via peachjar, an online platform for sending flyers to parents via their children's schools and community groups, and via word-of-mouth. Participants were healthy girls (sex and gender) with an age range of 9 to 16 years. Participants were required not to be pregnant, with no diagnosis of chronic pain, psychiatric or neurological disorders, disorders that are associated with pubertal maturation (eg, precocious puberty), disorders that can affect the endocrine system, and with no use of medications that affect the pain system or sex hormone levels (eg, opioids, hormone therapy).

2.2. Study design

The study design is depicted in **Figure 1**. The order of the tests was semirandomized and was from the least painful to the most painful to avoid a carryover effect that could affect the results of the next test. First, heat, cold, and pressure pain thresholds (PPT) were tested in a random order based on the participant ID number. Next, the familiarization part and temporal summation paradigm was completed. The tonic heat stimulus and offset analgesia paradigm were then delivered in a random order. After these tests, the conditioning stimuli part for the 2 conditioned pain modulation (CPM) paradigms were completed in a random order. An 8-minute break was kept between the tonic heat, offset analgesia, and CPM tests. The last test was the cold pain tolerance. During the breaks, participants completed surveys, including the Pubertal Developmental Scale (PDS). The investigator conducting the experimental pain assessments was blinded to the results of the PDS questionnaire and the participant's pubertal stage. At the end of the study visit and after completing the experimental pain measures, a blood draw was completed for analyses of sex hormone levels. The role of sex hormones on pain sensitivity in adolescents will be presented elsewhere.

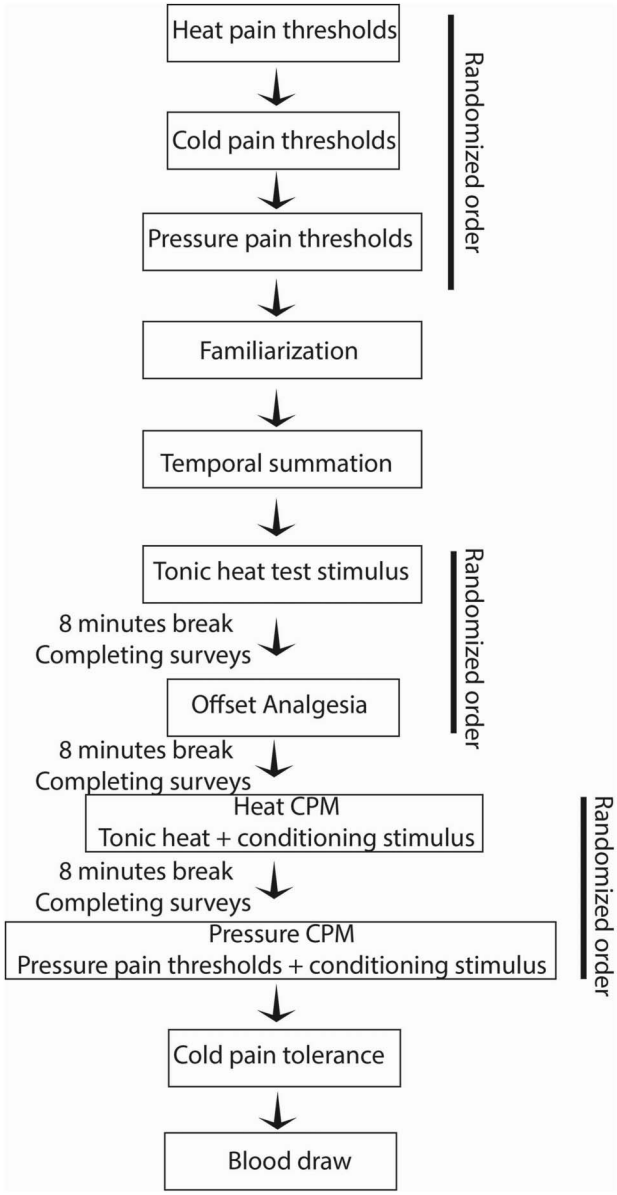

Figure 1. Study design. CPM, conditioned pain modulation.

2.3. Pubertal assessments

Pubertal maturation stage was assessed using the PDS questionnaire.[9] This survey has good reliability and validity and is correlated with Tanner staging.[9,26] Higher scores indicate a greater pubertal maturation stage. In addition, classification of the pubertal stages was done as follows: (1) prepuberty (score = 2, no menarche), (2) early-puberty (score = 3, no menarche), (3) mid-puberty (score > 3 and no menarche), (4) late-puberty (score ≤ 7, menarche), and (5) postpuberty (score = 8, menarche).[26] In addition, the PDS assesses self-perceived relative pubertal timing. Participants indicated if their pubertal maturation was much earlier, somewhat earlier, about the same, somewhat later, or much later compared with their peers. This approach is similar to previous studies that have used this

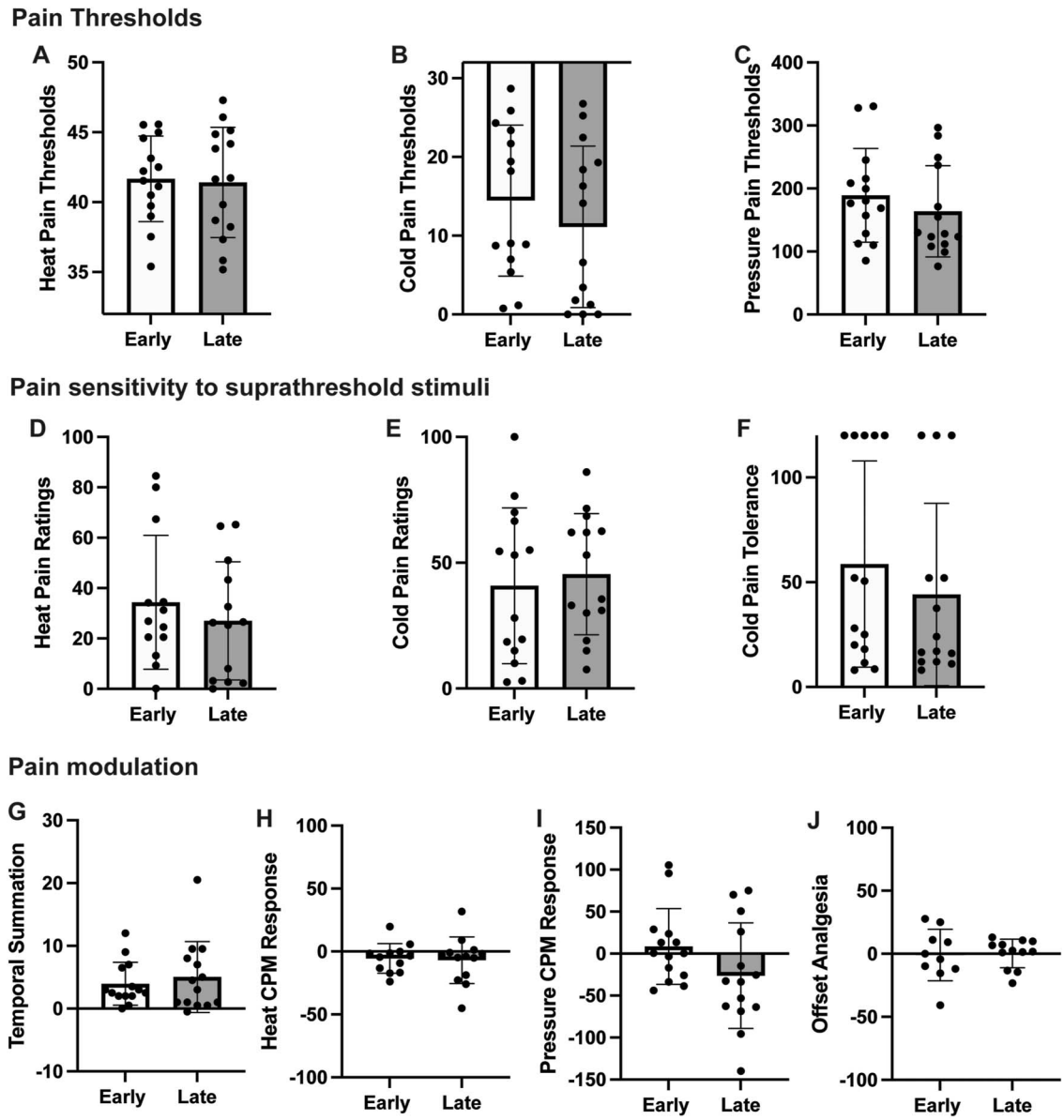

Figure 2. Experimental pain sensitivity between matched girls in early-mid vs. late pubertal maturation. Experimental pain sensitivity was compared between girls who are at the same age but at different pubertal maturation stage. No differences in experimental pain sensitivity were found between the groups. (A) Heat pain thresholds (°C); higher values indicate lower pain sensitivity. (B) Cold pain thresholds (°C); lower values indicate lower pain sensitivity. (C) Pressure pain thresholds (kPa); higher values indicate lower pain sensitivity. (D) Heat pain ratings (0–100) of the tonic heat test stimulus; lower values indicate lower pain sensitivity. (E) Cold pain ratings (0–100) of the conditioning stimulus; lower values indicate lower pain sensitivity. (F) Cold pain tolerance (seconds); higher values indicate lower pain sensitivity. (G) Temporal summation (delta of pain ratings of the 10th mechanical stimuli minus pain ratings of the first mechanical stimuli); negative values indicate lower excitatory response. (H) Heat CPM (delta of pain ratings of heat stimulus delivered together with the conditioning stimulus minus pain ratings of heat stimulus alone); negative values indicate more efficient inhibitory response. (I) Pressure CPM (delta of pressure pain thresholds alone minus pressure pain thresholds delivered together with the conditioning stimulus); negative values indicate more efficient inhibitory response. (J) Offset analgesia (delta of pain ratings of heat stimulus of the 46–47 − 46°C paradigm minus the pain ratings of heat stimulus of a constant 46°C); negative values indicate more efficient inhibitory response. CPM, conditioned pain modulation.

question to assess the subjective, perceived relative pubertal timing.[13,21,22]

2.4. Quantitative sensory testing

2.4.1. Heat and cold pain thresholds

The stimulus was delivered to the nondominant volar forearm using a 16 × 16-mm thermode (Medoc, Ramat Yishai, Israel). The temperature changed at a rate of 1.5°C/second and returned to a 32°C baseline at a rate of 6°C/second. Participants pressed a button the first moment they felt pain. Four heat and 4 cold pain threshold tests were completed, and the final scores were an average of the last 3 tests.

2.4.2. Pressure pain thresholds

Pressure pain threshold was delivered to the dominant trapezius with a pressure algometer (Medoc), using a 1-cm^2 probe and a rate of 60 kPa/second. Participants pressed a button the first moment they felt pain. Four PPT tests were completed, and the final score was an average of the last 3 tests.

2.4.3. Familiarization

Participants were familiarized with the stimuli and rating scales using a stimulus-response paradigm. The paradigm included applying 12 short 5-second, heat stimuli ranging from 39 to 47°C (39, 43, 44, 45, 46, and 47°C) to the dominant volar forearm and having participants rate their pain intensity and pain unpleasantness at the end of each stimulus. Each temperature was repeated twice, and the interstimulus interval was 30 seconds.

2.4.4. Temporal summation

A von Frey filament of 6.45 (a force of 180 gram) was delivered once and then 10 times to the nondominant volar forearm. Participants rated pain intensity after 1 stimulus and after 10 stimuli. Two temporal summation tests were conducted. The temporal summation value was the mean of the 2 tests calculated as the pain ratings of the 10th stimulus minus the pain ratings of the first stimulus. Positive values of temporal summation indicate an excitatory effect.

2.4.5. Conditioned pain modulation paradigm

Conditioned pain modulation is based on a "pain-inhibits-pain" concept that represents a spatial filtering mechanism that engages endogenous analgesia.[34,35] The test stimulus was delivered alone and then concurrently during the last 30 seconds of the conditioning stimulus. Two test stimuli were used in the study: PPT (see description above) and a tonic heat stimulus. The tonic heat stimulus was 46.0°C (a 16 × 16-mm thermode; Medoc) delivered to the nondominant volar forearm for 30 seconds. The baseline temperature was 35°C and the temperature increase/decrease rate was 6°C/second. Real-time pain intensity ratings were obtained using a Computerized Visual Analogue Scale (COVAS, Medoc), which ranges between "no pain sensation" to the "most intense pain imaginable." The conditioning stimulus was the immersion of the nondominant foot into a cold-water bath (8°C) for 60 seconds. Participants rated the conditioning cold stimulus pain intensity at the end of this stimulus using a mechanical VAS. During the last 30 seconds of the conditioning stimulus, the test stimulus was also delivered. The order in which the test stimuli were delivered together with the conditioning stimuli was randomized, and 8 minutes were kept between the tests to avoid carryover effects of the conditioning stimulus.[31] Heat CPM was calculated as the delta of heat pain ratings delivered together with the conditioning stimulus minus pain ratings of heat stimulus alone using absolute values. Pressure CPM was calculated as the delta of PPT alone minus PPT delivered together with the conditioning stimulus using absolute values. Negative values of the CPM response indicate an inhibitory effect.

2.4.6. Offset analgesia

In this paradigm, heat stimulus was delivered to the nondominant volar forearm using a 16 × 16-mm thermode. The offset analgesia stimulus consisted of 3 temperatures: 46°C for 5 seconds, 47°C for 5 seconds, and 46°C for 20 seconds. Participants continuously rated their pain intensity using the COVAS. Similar to a previous study,[34] the offset analgesia response was calculated as the difference between the mean pain intensity ratings of the time period between 13 and 23 seconds of the offset analgesia paradigm and the tonic heat stimulus of the CPM heat paradigm (constant 46°C for 30 seconds). Negative values of the offset analgesia response indicate an inhibitory effect.

2.4.7. Cold pain tolerance

Participants were asked to immerse their dominant foot in cold water (8°C) for as long as possible and until they could no longer hold their foot in the water. The cutoff duration was 120 seconds, after which participants were told to remove their foot from the water, and this duration was recorded as their cold pain tolerance.

2.5. Statistical analysis

The sample size calculation was based on group differences between girls in early vs late pubertal maturation and used unpublished pilot data from Cincinnati Children's Hospital Medical Center.[32,37] This study aimed to keep a narrow age range (80% were between 11 and 13 years) to distinguish pubertal vs age effects. However, even with this small age range, girls in early puberty were significantly younger than girls in late puberty, and it was not possible to differentiate puberty from age effects. Thus, we decided to use regression models. We calculated that with our sample size (n = 52), this study is powered to detect small size effects ($r^2 > 0.2$, alpha = 0.05 with 80% power, 2 predictors). Statistical analysis was performed using JMP Pro 16. Participants who could not tolerate the stimulation were excluded from that analysis (the exact numbers of participants included in each analysis are mentioned in the tables). Separate regression models were used to examine the effect of pubertal maturation stage, as indicated by the PDS scores and age on experimental pain sensitivity. Age and PDS score were moderately significantly correlated (r = 0.586, $P < 0.001$). However, it was below the threshold for collinearity (0.8); thus, they were included in the same model. In addition, the relationships between experimental pain sensitivity and menstrual phase and time since menarche were examined. Because these variables exist only for girls who are postmenarche and not in girls in early puberty who are premenarche, a dummy value of −1 was created for premenarche girls. The menstrual phase (days since the last period) and time since menarche (years) were not related to any of the experimental pain measures ($P > 0.05$) and, thus, were not controlled for in the models. Furthermore, we examined the relationships between experimental pain sensitivity and menstrual phase and time since menarche only in girls who are postmenarche (n = 26). No relationships between experimental pain measures and menstrual phase and time since menarche were found except for a relationship between cold pain tolerance and time since menarche ($r^2 = 0.194$, $P = 0.025$, without correction for multiple comparisons).

To better differentiate the role of puberty vs age, participants were categorized to prepuberty, early-puberty, mid-puberty, late-puberty, and postpuberty,[26] and pairs of adolescent girls who were of the same chronological age but at different pubertal stages (early-mid vs late) were identified. Experimental pain sensitivity was compared between the groups using *t*-tests. In addition, exploratory analyses to assess the subjective self-perceived pubertal timing were conducted using the relative puberty question in the PDS survey. Analyses of variance were used to compare experimental pain sensitivity between girls that their pubertal maturation is early (including the answers "much earlier" [n = 1] and "somewhat earlier" [n = 8]) vs same (n = 34) vs late (including the answers "somewhat later" [n = 7] and "much later" [n = 2]) relative to their peers. In addition, because of the unbalanced number of participants in the groups, *t*-tests were used to compare experimental pain sensitivity between girls that their pubertal maturation is early (n = 9) vs late (n = 9) relative to their peers.

3. Results

Fifty-two adolescent girls (mean age ± SD 12.0 ± 1.4 years, 37 Caucasians, 8 African Americans, 6 mixed race, and 1 Asian/Pacific Islander) completed the study. Participants were at prepuberty (n = 1), early-puberty (n = 6), mid-puberty (n = 18), late-puberty (n = 26), and postpuberty (n = 1). Using the PDS scores as a continuous variable and age, regression analyses found no relationships between the PDS scores and experimental pain sensitivity, even without correcting for multiple comparisons (**Table 1**). For age, a significant effect was found only for cold pain tolerance ($P = 0.030$, **Table 1**), indicating that older girls have lower experimental pain sensitivity demonstrated by higher cold pain tolerance. This relationship was not significant after correction for multiple comparisons.

To differentiate between the effects of pubertal maturation and age, additional analyses were conducted in which experimental pain sensitivity was compared between adolescent girls of the same age but at different pubertal stages (early-mid vs late). Because age was identical, these analyses allowed distinguishing the effects of puberty from age. Twenty-eight girls were included in this analysis (14 early-mid and 14 late, mean age for both groups was 12.0 ± 0.7 years). No differences in any of the experimental pain measures were found (**Table 2**, **Fig. 2**), suggesting no effect of pubertal maturation on experimental pain sensitivity.

The effect of subjective, relative pubertal timing (ie, if the individual perceives herself as nonnormative in her development, either early or late, compared wih her peers) on experimental pain sensitivity was also examined. Nine girls indicated their pubertal maturation was early relative to their peers, 34 indicated their pubertal maturation was similar to their peers, and 9 girls indicated their pubertal maturation was late relative to their peers. No differences in experimental pain sensitivity were found between the groups (**Table 3**). When only girls in early and late relative pubertal maturation were compared, similar results were found with no differences in experimental pain sensitivity (**Table 3**).

4. Discussion

This study focused on the role of puberty in experimental pain and found overall no effects of pubertal stage and age on experimental pain sensitivity, using a comprehensive assessment that includes pain thresholds, pain ratings to heat and cold stimuli, and pain modulation tests. Furthermore, no differences in experimental pain sensitivity were found between girls of the same age but at different pubertal maturation stages (early-mid vs late) or between girls at different pubertal timing relative to their peers. Thus, these results suggest that factors other than age and

Table 1

Pubertal maturation and age effects on experimental pain sensitivity in healthy girls.

	Estimate	Std error	T ratio	Significance
Pain thresholds				
Heat pain thresholds (n = 52, $r^2 = 0.027$)				
PDS score	0.418	0.421	0.99	0.325
Age	−0.041	0.401	−0.10	0.920
Cold pain thresholds (n = 52, $r^2 = 0.018$)				
PDS score	−0.726	1.315	−0.55	0.584
Age	−0.388	1.254	−0.31	0.758
Pressure pain thresholds (n = 52, $r^2 = 0.065$)				
PDS score	10.246	9.472	1.08	0.285
Age	5.237	9.033	0.58	0.565
Pain sensitivity to suprathreshold stimuli				
Heat pain ratings (n = 44, $r^2 = 0.061$)				
PDS score	1.848	3.588	0.52	0.609
Age	−5.539	3.522	−1.57	0.123
Cold pain ratings (n = 52, $r^2 = 0.056$)				
PDS score	0.512	0.362	1.41	0.163
Age	−0.554	0.345	−1.61	0.115
Cold pain tolerance (n = 52, $r^2 = 0.097$)				
PDS score	−4.663	5.421	−0.86	0.394
Age	11.532	5.170	2.23	0.030*
Pain modulation				
Temporal summation (n = 52, $r^2 = 0.085$)				
PDS score	−0.042	0.087	−0.48	0.632
Age	−0.115	0.083	−1.40	0.169
Heat CPM (n = 43, $r^2 = 0.064$)				
PDS score	−3.137	2.360	−1.33	0.191
Age	−0.136	2.325	−0.06	0.954
Pressure CPM (n = 51, $r^2 = 0.006$)				
PDS score	−2.800	6.621	−0.42	0.674
Age	3.178	6.278	0.51	0.615
Offset analgesia (n = 39, $r^2 = 0.038$)				
PDS score	−1.657	2.968	−0.56	0.580
Age	−1.564	2.859	−0.55	0.588

Heat pain ratings (0–100) of the tonic heat test stimulus; cold pain ratings (0–100) of the conditioning stimulus; temporal summation (delta of pain ratings of the 10th mechanical stimuli minus pain ratings of the first mechanical stimuli), negative values indicate lower excitatory response; heat CPM (delta of pain ratings of heat stimulus delivered together with the conditioning stimulus minus pain ratings of heat stimulus alone), negative values indicate more efficient inhibitory response; pressure CPM (delta of pressure pain thresholds alone minus pressure pain thresholds delivered together with the conditioning stimulus), negative values indicate more efficient inhibitory response; and offset analgesia (delta of pain ratings of heat stimulus of the 46–47 − 46°C paradigm minus the pain ratings of heat stimulus of a constant 46°C), negative values indicate more efficient inhibitory response.

* This relationship was not significant after correction for multiple comparisons, which requires $P < 0.005$.

CPM, conditioned pain modulation; PDS, pubertal developmental scale.

Table 2

Experimental pain sensitivity in *matched* girls in early-mid vs late pubertal maturation.

	Early-mid puberty (n = 14)	Late puberty (n = 14)	95% CI diff	*P*
Pain thresholds				
Heat pain thresholds (°C)	41.7 ± 3.1	41.4 ± 3.9	−3.0, 2.5	0.852
Cold pain thresholds (°C)	14.5 ± 9.6	11.1 ± 10.2	−11.1, 4.4	0.381
Pressure pain thresholds (kPa)	189.1 ± 74.3	163.8 ± 72.4	−82.3, 31.7	0.371
Pain sensitivity to suprathreshold stimuli				
Pain ratings of heat stimulus (VAS 0–100, n = 13)	34.4 ± 26.6	27.0 ± 23.5	−27.7, 12.9	0.461
Pain ratings of cold stimulus (VAS 0–100)	40.9 ± 31.0	45.5 ± 24.0	−17.0, 26.2	0.664
Cold pain tolerance (s)	58.7 ± 49.2	44.1 ± 43.5	−50.6, 21.6	0.415
Pain modulation				
Temporal summation (ΔVAS)	4.0 ± 3.4	5.0 ± 5.7	−2.6, 4.7	0.551
Heat CPM response (ΔVAS, n = 12)	−5.5 ± 11.7	−8.2 ± 18.7	−16.1, 10.6	0.674
Pressure CPM response (ΔkPa)	8.5 ± 45.1	−26.3 ± 62.9	−77.5, 8.0	0.106
Offset analgesia (ΔVAS, n = 9)	−4.1 ± 18.8	1.1 ± 9.5	−10.2, 20.6	0.474

Data is resented as mean ± SD.
CPM, conditioned pain modulation; VAS, visual analogue scale.

pubertal maturation may affect experimental pain sensitivity in healthy adolescent girls.

Generally, it is difficult to distinguish between puberty-related and age-related effects as age and puberty are highly correlated (ie, older girls are typically more mature). Previous studies mostly focused on age and found that older adolescents (who were probably also more mature) have lower pain sensitivity, but whether it is an age effect or pubertal effect could not be determined.[3,4,29,42,44] In this study, age and puberty were only moderately correlated, potentially because of the focus on a relatively small age range (80% of participants were between age 11 and 13 years). The small age range allowed conducting a targeted subanalysis that distinguished between age and puberty by identifying pairs of girls of the same age but at different pubertal statuses. In these analyses, in which age was identical, and girls differed only in the pubertal stage, no differences were found between the groups, confirming the findings of no effect of puberty on individual differences in experimental pain in healthy adolescent girls.

This study found that age was related only to cold pain tolerance, although this was no longer significant after correction for multiple comparisons. One previous study assessed cold pain tolerance in adolescents grouped by age (9–11, 12–14, and 15–17 years) and similarly found that older adolescents had a greater cold pain tolerance.[39] However, the lack of relationships between age and the other experimental pain measures may contradict other adolescent studies, which found age effects on experimental pain sensitivity (eg, cold pain thresholds, heat pain thresholds, pressure pain thresholds, mechanical pain thresholds, and temporal summation).[3,4,39,43] This could be due to the different analysis approach and/or the relatively narrow age range: in this study, most participants were between age 11 and 13 years, while children and adolescents with a larger age range participated in the previous studies. With this narrow age range, there may be only a small variability in the biopsychosocial factors such as sex hormones, neural function, mood, and relationships with peers and family. These factors change with age/puberty and can affect pain.[2,7,15,20,33,36,47] A larger age difference may be related to a larger interindividual variability in these biopsychosocial factors that could affect pain sensitivity. Future studies are needed to identify which biopsychosocial factors may contribute to pubertal/age-related differences in pain to identify new potential interventions for pediatric pain.

This study included an exploratory analysis to assess the subjective self-perceived pubertal timing (subjective feeling of nonnormal maturation relative to same-age peers).[10] Developing early or later compared with peers could result in an increased risk of depression and internalizing symptoms,[14,40,45] which is related to greater pain sensitivity.[1,17] Thus, both relative early and relative late pubertal maturation may result in higher pain sensitivity, which could

Table 3

Experimental pain sensitivity in girls in relative early vs relative late pubertal maturation.

	Relative early (n = 9)	Same (n = 34)	Relative late (n = 9)	3-way ANOVA (*P*)	T-test relative early vs relative late (*P*)
Age (y)	12.4 ± 1.1	11.8 ± 1.6	12.2 ± 1.0	0.449	0.661
PDS score	2.9 ± 0.7	2.6 ± 0.7	2.3 ± 0.7	0.203	0.075
Pain thresholds					
Heat pain thresholds (°C)	43.3 ± 3.0	41.7 ± 3.0	41.4 ± 4.4	0.354	0.305
Cold pain thresholds (°C)	13.9 ± 10.4	13.1 ± 10.0	10.1 ± 11.3	0.680	0.462
Pressure pain thresholds (kPa)	191.2 ± 78.6	163.8 ± 70.9	171.2 ± 90.5	0.629	0.622
Pain sensitivity to suprathreshold stimuli					
Pain ratings of heat stimulus (VAS 0–100)	36.0 ± 30.6	33.0 ± 27.4 (n = 28)	18.3 ± 14.9 (n = 7)	0.364	0.153
Pain ratings of cold stimulus (VAS 0–100)	49.3 ± 29.2	39.4 ± 27.0	38.4 ± 35.1	0.636	0.485
Cold pain tolerance (s)	37.3 ± 36.7	45.7 ± 45.0	63.2 ± 45.2	0.433	0.202
Pain modulation					
Temporal summation (ΔVAS)	6.3 ± 5.5	4.1 ± 4.5	8.3 ± 13.2	0.236	0.690
Heat CPM response (ΔVAS)	−9.9 ± 17.7	−5.2 ± 19.0 (n = 27)	−6.2 ± 11.4 (n = 7)	0.793	0.617
Pressure CPM response (ΔkPa)	6.7 ± 39.7	−19.0 ± 54.0 (n = 33)	4.8 ± 41.2	0.246	0.920
Offset analgesia (ΔVAS)	−14.1 ± 22.0 (n = 8)	−3.7 ± 21.9 (n = 25)	−4.7 ± 11.1 (n = 6)	0.472	0.319

Data are presented as mean ± SD.
ANOVA, analysis of variance; CPM, conditioned pain modulation; PDS, pubertal developmental scale; VAS, visual analogue scale.

explain the findings of the lack of differences in experimental pain sensitivity between these 2 groups. However, no effects of perceived relative puberty on experimental pain were observed. Notably, this analysis included a small number of participants, as most participants reported similar pubertal maturation compared with their peers. In addition, although using the PDS survey to assess the subjective self-perceived pubertal timing is common,[13,21,22] several previous studies used a different approach to calculate pubertal timing, such as comparing the PDS scores to the average scores of the other study participants who were at the same age and sex and even the same school class.[40,45] However, this approach was not feasible in this study, which included participants of different ages who did not know each other. Thus, this study assessed the participant's perception of her development (same vs different from peers) without testing whether the participant's perception is objectively accurate.

Although puberty is a critical period in life related to many changes in experimental and clinical pain, only a few studies comprehensively examined the role of puberty on pain. A key limitation of this study is the relatively small sample, although our sample size allowed us to detect even effects of small size. Nonetheless, even without correcting for multiple comparisons, no relationships were found between pubertal maturation and experimental pain sensitivity. In addition, there are several methods to assess pubertal stages, with Tanner staging being the gold standard.[12,18,19,30] In this study, the self-reported PDS questionnaire was used, which is more feasible and widely used in research settings and is significantly correlated with Tanner staging.[8,26,41] Importantly, this study used a cross-sectional design and, thus, could not conclude how changes in pubertal maturation/age relate to changes in experimental pain sensitivity. Furthermore, adolescents at different pubertal maturation stages/ages may differ in biopsychosocial factors such as sex hormone levels.[2,25] Thus, the role of biopsychosocial factors on experimental pain sensitivity still needs to be examined. Finally, this study focused on girls, and future studies are needed to examine the study aims in boys.

To conclude, this study found overall no effects of pubertal stage and age on experimental pain sensitivity and modulation in healthy girls. Greater effects on experimental pain sensitivity may be found in adolescents with a large age difference, who may have greater individual variability in the biopsychosocial factors that change with age/puberty and can affect pain sensitivity.

Disclosures

The authors have no conflict of interest to declare.

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