Headache Medicine

DOI: 10.48208/HeadacheMed.2025.24



Original

Migraine in children and adolescents: the clinical impact of allodynia

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Edited by:

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Introduction

The pathophysiology of migraine is strongly associated with central sensitization, the presence of which is related to cutaneous allodynia and cervical musculoskeletal dysfunction. However, these aspects remain understudied in children and adolescents. Thus, this study aimed to evaluate differences in clinical variables, sensitization, and musculoskeletal alterations between children (CR) and adolescents (AD) with migraine, considering the presence or absence of cutaneous allodynia.

Methods

One hundred and one participants aged 6 to 16 years with a clinical diagnosis of migraine were evaluated. Outcomes included cervical range of motion (ROM), pressure pain threshold (PPT) of cranio-cervical muscles, and presence of cutaneous allodynia.

Results

Significant differences were observed between CR and AD for age (p<0.001) and PPTs of the sternocleidomastoid (p=0.002), levator scapulae (p=0.006), suboccipital (p=0.006), trapezius (p<0.001), and anterior scalene (p<0.001) muscles. The subgroups CR and AD with and without allodynia showed significant differences in the PPTs of the sternocleidomastoid (p=0.020), levator scapulae (p=0.016), suboccipital (p=0.038), trapezius (p<0.001), anterior scalene (p<0.001) muscles, and in cervical ROM in the sagittal plane (p=0.016). The main differences were observed between adolescents and children with and without allodynia. No differences were found within the children and adolescents' subgroups.

Conclusion

The presence of cutaneous allodynia is associated with increased muscle sensitivity and reduced cervical sagittal mobility. These findings highlight the importance of early assessment of allodynia and musculoskeletal sensitivity in children and adolescents with migraine.

Keywords:

Migraine Neck mobility Cutaneous allodynia

> Received: August 29, 2025 Revised: September 23, 2025 Accepted: September 29, 2025





Introduction

Globally, more than 60% of children and adolescents experience headaches. Of those, 7.7% to 9.1% are diagnosed with migraine, which is a primary headache disorder that affects both adults and children and share common symptoms (1,2). However, migraine attacks in children tend to be of shorter duration and may affect both sides of the head (3). Importantly, even among children, migraine is recognized as a disabling condition that negatively impact quality of life, academic performance, and leisure activities (4,5).

Migraine is a chronic neurological disease primarily involving central sensitization of the trigeminocervical system. This system receives afferent input from the trigeminal and upper cervical nerves that innervate meningeal vessels, the face, and cervical structures. During migraine attacks, meningeal inflammation occurs, accompanied by the release of inflammatory neuropeptides, such as calcitonin gene-related peptide CGRP and substance P. Due to the convergence of trigeminal and cervical sensory input, pain may radiate to the neck region (5).

In adult with migraine, this relationship is supported by evidence of increased muscle tenderness (7), reduced muscular endurance, and restricted cervical range of motion (8). In populations of children and adolescents, evidence also suggests increased muscle sensitivity, with lower pressure pain thresholds in pericranial, neck, and shoulder muscles when compared to children and adolescents without headaches or with tension-type headache (9). However, the cervical range of motion in this age group has been minimally investigated, with only one study of adolescents reporting no significant differences in cervical mobility (10).

One clinical presentation of central sensitization is cutaneous allodynia, which is defined as pain or discomfort caused by normally non-noxious stimuli to the skin (11). In adult with migraine, cutaneous allodynia has been associated with reduced cervical strength (12), an increased risk of migraine chronification, the presence of neck pain, and poorer clinical outcomes (13). Approximately 16% of children and adolescents with pediatric migraine report cutaneous allodynia (14), which is significantly higher than the prevalence among those with other primary headache disorders (37% vs. 0%) (15). Levinsky et al. (2019) reported allodynia predominantly among girls in a children and adolescents' sample (16). Moreover, compared to adults, cutaneous allodynia in children and adolescents has been associated with physical activity-induced pain exacerbation, phonophobia, nausea, migraine with aura, and being awakened by pain (17).

Musculoskeletal manifestations observed in adults support the hypothesis that migraine may involve not only central mechanisms but also peripheral components (6). Since migraine is a chronic neurobiological condition that persists throughout life, it is reasonable to assume that these alterations may be present from childhood, albeit with age-specific characteristics. Furthermore, longitudinal studies indicate that an early onset of migraine attacks may be a poor prognostic factor, increasing the likelihood of persistent migraine frequency and allodynia symptoms in adulthood (18).

Therefore, the early investigation of signs of central sensitization and its peripheral manifestations, such as allodynia and cervical dysfunction, and their potential associations, may offer insights into migraine activity and its impact in children and adolescents. This may aid in identifying subgroups with greater functional vulnerability, paving the way for earlier and more targeted therapeutic strategies. However, no previous studies have examined the relationships between clinical migraine characteristics, cervical range of motion, and pressure pain thresholds in the cervical muscles of children and adolescents with and without allodynia.

Thus, considering the potential impact of allodynia in adults and its documented presence in children and adolescents with migraine, this study aimed to conduct an exploratory analysis to assess differences in clinical, sensitization, and musculoskeletal variables between children and adolescents, due to their biological differences, with and without cutaneous allodynia and a diagnosis of migraine.

Methodology

Study sample

This is a cross-sectional study involving secondary data analysis derived from two distinct projects, both previously approved by the local Research Ethics Committee (CAAE: 70680023.6.0000.5440 and CAAE: 31864020.0.0000.5440). The datasets were combined to enhance statistical power and explore common variables between the studies. All participants provided informed assent appropriate for their age group, and their parents or legal guardians signed the informed consent form with detailed information about the study.

A total of 101 children (CH) and adolescents (AD) aged between 6 and 16 years, diagnosed with migraine by a neurologist specialized in headache disorders, were included based on the criteria of the International Classification of Headache Disorders - Third Edition (ICHD-III). Participants aged up to 11 years were classified as children, and those between 12 and 18 years as adolescents. Assessments were conducted between October 2023 and August 2024. Patients were recruited by convenience from the



tertiary care Pediatric Headache Clinic of the Ribeirão Preto Medical School Hospital and were required to report at least three headache episodes per month (3). Exclusion criteria included a concurrent or inconclusive diagnosis of other headache types, neuromuscular or orthopedic conditions, attention deficit disorders, or inability to comprehend and follow instructions.

Physical assessment and auestionnaire

Participants were evaluated by two trained assessors who conducted a structured anamnesis collecting sociodemographic data, headache frequency (days/month), pain intensity (numerical pain scale), use of preventive or abortive medications, craniocervical physical tests to assess pressure pain threshold (PPT) and cervical range of motion (ROM), and a children and adolescents-adapted version of a cutaneous allodynia questionnaire previously used in children and adolescents populations (15,16).

Pressure Pain Threshold (PPT) assessment

PPT was assessed using a digital algometer (DDK-20, Kratos) and a digital metronome set at 1 Hz to provide auditory feedback and standardize the application rate of pressure by the examiner (7,10). The initial pressure applied was 0.1 kg/cm², followed by a constant pressure rate of 0.5 kg/cm²/s. Prior to testing, participants underwent familiarization with the algometer using pressure applied to the thenar eminence of the right hand. This method has shown moderate to excellent reliability in children and adolescents' populations (19).

Anatomical landmarks were selected based on previous studies with adult with migraine (7), which identified reduced PPT in the following muscles: sternocleidomastoid (SCM), levator scapulae, suboccipital, upper trapezius, and anterior scalene. Muscles were identified through anatomical analysis and palpation, marked bilaterally in random order, and tested in two consecutive series separated by five minutes (10). All instructions were delivered in age-appropriate language to ensure comprehension. Assessments were performed as efficiently as possible to minimize discomfort and distraction.

Cervical Range of Motion (ROM) assessment

Cervical ROM was assessed using the CROM® – Performance Attainment Associates, St. Paul, MN, USA device to measure active range in the cervical flexion, extension, lateral flexion, and rotation planes (20). Participants were seated comfortably with feet flat on the floor, hips, knees, and ankles at 90°, back supported, and arms resting on the thighs. The CROM device was positioned according to the manufacturer's instructions.

Participants were instructed to perform maximal cervical flexion, extension, right/left lateral flexion, and right/left rotation in random order. Standardized verbal instructions were used for each movement (20). The CROM® device has demonstrated excellent reliability for assessing cervical ROM in children and adolescents (21).

Cutaneous Allodynia Questionnaire (ICHD-III Beta Adapted Version)

To identify the presence of cutaneous allodynia in migraineurs, a freely translated and adapted version of a four-item questionnaire was used. It assessed discomfort triggered by daily activities during migraine attacks, including wearing objects on the neck or head. The presence of allodynia was confirmed if participants answered affirmatively to at least one item (22). For younger children, parents or legal guardians contributed by reporting observations of their child's behavior during migraine episodes.

Statistical analysis

Means and standard deviations were calculated for continuous variables, while absolute and relative frequencies were reported for clinical and sociodemographic characteristics. The Shapiro-Wilk test was used to assess the normality of the data. For continuous variables, independent samples t-tests were applied when comparing two group means with normal distribution, and one-way analysis of variance (ANOVA) was used for comparisons among three or more groups. When assumptions of normality were not met, the Mann-Whitney test or Kruskal-Wallis test (>3 independent groups) was employed. For categorical variables, Pearson's chi-square test or Fisher's exact test was used, depending on the expected frequency in the cells. Post hoc Dunn's test was applied for multiple comparisons following the Kruskal-Wallis test in subgroup analyses. All statistical analyses were performed using SPSS software, version 24.0.

Results

The data revealed significant differences between the CH and AD groups in terms of age (p<0.001) and pressure pain thresholds (PPTs) of the sternocleidomastoid (SCM) (p=0.002), levator scapulae (p=0.006), suboccipital (p=0.006), trapezius (p<0.001), and anterior scalene muscles (p<0.001). No significant differences were found between groups regarding demographic variables, presence of allodynia, migraine diagnosis, engagement in physical activity, headache frequency and intensity, use of abortive or prophylactic medication, or cervical range of motion (ROM) (p>0.05) (Table 1).



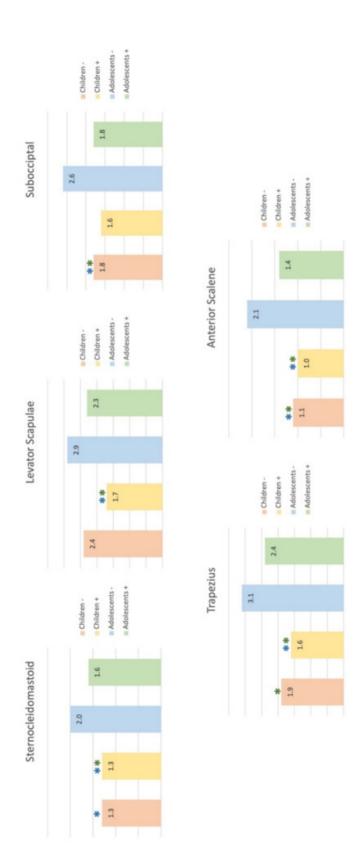
Table 1. Differences between children and adolescents with migraine (n=101)

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	CR (n=51)	AD (n=50)	p-value	
Female sex (n/%)	34 (66.7)	26 (52.0)	0.097%	
Age (years)	8.9 (1.7)	13.7 (1.6)	<0.001#	
Allodynia (n/%)	33 (64.7)	31.7 (62.0)	0.470%	
Diagnosis (n/%)				
MoA	36 (70.6)	31 (62.0)		
MA	13 (25.5)	15 (30.0)	0.556+	
CM	2 (3.9)	4 (8.0)		
Physical activity (n/%)	26 (51.0)	21 (42.0)	0.240%	
Headache frequency	8.5 (6.1)	8.9 (6.8)	0.965#	
Headache intensity (n/%)				
Mild	2 (3.9)	3 (6.0)		
Moderate	19 (37.3)	14 (28.0)	0.580 ⁺	
Severe	30 (58.8)	33 (66.0)		
Abortive medication (n/%)	48 (94.1)	47 (94.0)	0.652%	
Prophylactic medication (n/%)	37 (72.5)	35 (70.0)	0.475%	
PPT (kg/cm²)				
SCM	1.3 (0.4)	1.7 (0.9)	0.002#	
Levator scapulae	1.9 (1.1)	2.5 (1.7)	0.006#	
Suboccipital	1.6 (0.8)	2.1 (1.5)	0.006#	
Trapezius	1.7 (0.8)	2.7 (1.7)	<0.001#	
Scalene	1.1 (0.6)	1.7 (1.4)	<0.001#	
ROM (degrees)				
Frontal plane	94.8 (13.7)	92.3 (13.3)	0.177#	
Sagittal plane	136.2 (24.5)	131.2 (22.8)	0.204#	
Transverse plane	146.2 (17.6)	140.6 (18.2)	0.117*	

MoA: Migraine without aura; MA: Migraine with aura; CM: Chronic migraine; PPT: Pressure pain threshold; SCM: Sternocleidomastoid; ROM: Range of motion. *Independent t test; #Mann-Whitney test; "Pearson's chi-square; +Fisher's exact test."

When stratifying the sample into CH and AD subgroups with and without allodynia, significant differences were observed in the PPTs of the SCM (p=0.020), levator scapulae (p=0.016), suboccipital (p=0.038), trapezius (p<0.001), and anterior scalene muscles (p<0.001), as well as in sagittal plane ROM (p=0.016). These differences are illustrated in Figure 1. No significant differences were found among other clinical and demographic variables (p>0.05) (Table 2).





Green asterisk is the difference compared to the adolescents with cutaneous allodynia group. Blue asterisk is the difference compared to the adolescents without cutaneous Figure 1. Graphical representation of differences in pressure pain thresholds (PPT) of cervical muscles in children and adolescents with (+) and without (-) cutaneous allodynia. allodynia group.



Table 2. Clinical and sociodemographic characteristics of children and adolescents with and without allodynia (n=101)

	CH-(n=18)	CH+(n=33)	AD-(n=19)	AD+(n=31)	p-value
Diagnosis (n/%)					
MoA	15 (83.3)	21 (63.6)	12 (63.2)	19 (61.3)	0.737+
MA	3 (16.7)	10 (30.3)	5 (26.3)	10 (32.3)	
CM	0 (0.0)	2 (6.1)	2 (10.5)	2 (6.5)	
Physical activity (%)	9 (50.0)	17 (51.5)	7 (36.8)	14 (45.2)	0.763%
Headache frequency	8 (4.9)	8.8 (6.8)	8.6 (7.8)	9 (6.3)	0.907&
Headache intensity (n/%)					0.532+
Mild	0 (0.0)	2 (6.1)	1 (5.3)	2 (6.5)	
Moderate	7 (38.9)	12 (36.4)	8 (42.1)	6 (19.4)	
Severe	11 (61.1)	19 (57.6)	10 (52.6)	23 (72.2)	
Abortive use (n/%)	17 (94.4)	31 (93.9)	18 (94.7)	29 (93.5)	0.998%
Prophylactic use (n/%)	10 (55.6)	27 (81.8)	11 (57.9)	24 (77.4)	0.102%
PPT (kg/cm²)					
SCM	1.3 (0.4) ^b	1.3 (0.4) ^{d,e}	2.0 (1.3)	1.6 (0.6)	0.020&
Levator scapulae	2.4 (1.6)	1.7 (0.6) ^{d,e}	2.9 (2.5)	2.3 (0.9)	0.016 ^{&}
Suboccipital	1.8 (1.2) ^b	1.6 (0.6) ^d	2.6 (2.2)	1.8 (0.7)	0.038&
Trapezius	1.9 (1.0) ^c	1.6 (0.6) ^{d,e}	3.1 (2.5)	2.4 (1.0)	<0.001&
Scalene	1.1 (0.8) ^{b,c}	1.0 (0.4) ^{d,e}	2.1 (2.1)	1.4 (0.5)	<0.001&
ROM (degrees)					
Frontal plane	97.3 (11.0)	93.3 (15.0)	94.7 (14.0)	90.8 (12.9)	0.388&
Sagittal plane	147.6 (20.7) ^{a,b,c}	130.1 (24.5)	129.5 (28.3)	132.2 (19.1)	0.016&
Transverse plane	152.3 (14.6)	142.9 (18.4)	138.8 (20.5)	141.6 (16.9)	0.111\$

CH-: child without allodynia; CH+: child with allodynia; AD-: adolescent without allodynia; AD+: adolescent with allodynia; MoA: Migraine without aura; MA: Migraine with aura; CM: Chronic migraine; PPT: pressure pain threshold; SCM: sternocleidomastoid; ROM: range of motion Pairwise comparisons: °CH- vs. CH+; b CH- vs. AD-; °CH- vs. AD-; °CH+ vs. AD-



Discussion

The data indicate that both children and adolescents with migraine exhibited similarities regarding female predominance and a high frequency of cutaneous allodynia (64.7% in CH and 62.0% in AD). Most individuals were classified as having episodic migraine, with severe headache attacks reported in over 58% of cases. The majority used both abortive and preventive medications. Interestingly, children exhibited lower pressure pain thresholds (PPT) than adolescents, regardless of the presence of allodynia. When considered with and without allodynia subgroups, significant differences were observed in sagittal plane cervical ROM.

Previous cross-sectional studies have reported that approximately 16% of children and adolescents with migraines experience symptoms of cutaneous allodynia. The present study found considerably higher prevalence rates (64.7% in CH and 62.0% in AD), which reinforces the idea that headache attacks and allodynia are more intense and prevalent among migraineurs than in the general population or individuals with other types of primary headache (15,17). These findings support the hypothesis that central sensitization substantially influences pain perception, even in children and adolescents with migraine.

Thus, this study underscores the importance of evaluating the presence of allodynia in children and adolescents with migraine, given its high prevalence and considering that, in adults, allodynia is already associated with poorer response to abortive medication, worse clinical prognosis, and increased risk of migraine chronification (23) Early identification and management of allodynia in childhood may therefore be critical.

According to the findings of this article, the subgroup of children differs from adolescents in relation to craniocervical pain perception, regardless of the presence of cutaneous allodynia. The reduced pain thresholds observed in children suggest a greater degree of central sensitization in this age group, meaning low-intensity stimuli can be painful (24). It is important to emphasize that the central nervous system in children is still maturing (25), which may contribute to heightened hypersensitivity because processing pathways are not yet fully developed. This phenomenon appears to be more pronounced in girls. According to the literature, girls tend to have lower pain pressure thresholds (PPT) and may be more prone to persistent patterns of central sensitization throughout life. This increases their risk of chronic migraines in adulthood (26). The findings from this study are consistent with this evidence and underscore the importance of assessing PPTs and implementing therapeutic strategies that target both central and peripheral sensitization.

Regarding musculoskeletal dysfunction, cervical range of motion differs between chronic headache and acute headache groups with and without allodynia only in the sagittal plane, composed by flexion and extension movements. Previous studies have found no significant differences in cervical mobility among adolescents with migraines, tension-type headaches, and control subjects (10). However, contrary to these earlier findings, our study observed significant differences in cervical ROM among children and adolescents with and without allodynia, particularly in flexion and extension movements. While values remained within the normative range for this age group (27), the observed reductions in these movements, especially in association with allodynia, suggest a potential early involvement of musculoskeletal dysfunction associated to central sensitization.

This is a novel finding for children and adolescents with migraine. While altered muscular performance is well documented in adults with migraine (28), in children and adolescents with allodynia, musculoskeletal impairments appear more localized to muscles responsible for sagittal plane movement. This reinforces the need to include cervical ROM assessment in the clinical evaluation of children and adolescents with migraine, particularly in the presence of allodynia.

The present findings suggest that allodynia influences both muscular sensitivity and sagittal plane cervical mobility in children and adolescents with migraine. Therefore, therapeutic strategies aimed at modulating central and peripheral sensitization may play a role in reducing pain and preventing migraine chronification in adulthood (29). Limitations and Strengths

This study has limitations. The sample was drawn from a tertiary care center, limiting generalizability to patients with similar clinical profiles. Despite the data collection was done at the hospital, the inclusion and exclusion criteria were met to guarantee the diagnosis of migraine and exclude comorbidities that may have some influence at the final result. The allodynia questionnaire used was adapted for children without formal validation, which may impact the accuracy of allodynia identification; however, it remains the only tool currently available and widely used in children and adolescents with migraine research.

Despite these limitations, the study has several strengths. It employed reliable instruments for measuring PPT and cervical ROM, with assessments conducted by trained professionals, ensuring high methodological rigor. Including a clinically well-defined sample diagnosed by headache specialists adds credibility to the findings. Furthermore, this study is the first to identify potential associations between allodynia, muscle sensitivity, and cervical mobility in children and adolescents with migraine.



Conclusion

Cutaneous allodynia, which was prevalent in both groups of children and adolescents, was associated with increased muscle sensitivity and decreased cervical range of motion in the sagittal plane. These results highlight the importance of promptly assessing allodynia sensitivity and musculoskeletal disorders in children and adolescents with migraine. This assessment is important for developing therapeutic strategies that target central sensitization and prevent the worsening of the disease.

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Declarations of interest: The authors declare no conflict of interest.

Authors Contributions: JP, AM, AR, DBG: Conception, design, analysis, interpretation of data for the work, drafting the working, reviewing and final approval; FDS,VCL: Drafting the working, reviewing and final approval. NVS: Acquisition of data, drafting the working, reviewing and final approval. FD: Acquisition of data, reviewing and final approval.

Funding: This research was supported by the São Paulo Research Foundation (FAPESP), grant number 2023/09538-5 and in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001.