

Psychosocial and psychophysical assessment in paediatric patients and young adults with chronic back pain: A cluster analysis

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Abstract

Background: Identifying subgroups with different clinical profiles may inform tailored management and improve outcomes. The objective of this study was to identify psychosocial and psychophysical profiles of children and adolescents with chronic back pain.

Methods: One hundred and ninety-eight patients with chronic back pain were recruited for the study. Pain assessment was mainly conducted in the form of an interview and with the use of validated pain-related questionnaires assessing their psychosocial factors and disability. All patients underwent mechanical and thermal quantitative sensory tests assessing detection and pain thresholds, and conditioned pain modulation efficacy.

Results: Hierarchical clustering partitioned our patients into three clusters accounting for 34.73% of the total variation of the data. The adaptive cluster represented 45.5% of the patients and was characterized to display high thermal and pressure pain thresholds. The high somatic symptoms cluster, representing 19.2% of patients, was characterized to use more sensory, affective, evaluative and temporal descriptors of pain, more likely to report their pain as neuropathic of nature, report a more functional disability, report symptoms of anxiety and depression and report poor sleep quality. The pain-sensitive cluster, representing 35.4% of the cohort, displayed deep tissue sensitivity and thermal hyperalgesia.

Conclusions: This study identified clinical profiles of children and adolescents experiencing chronic back pain based on specific psychophysical and psychosocial characteristics highlighting that chronic pain treatment should address underlying nociceptive and non-nociceptive mechanisms.

Significance: To our current knowledge, this study is the first to conduct cluster analysis with youth experiencing chronic back pain and displays clinical profiles based on specific physical and psychosocial characteristics. This study highlights

that in a clinical context, chronic pain assessment should include multiple elements contributing to pain which can be assessed in a clinical context and addressed when pathoanatomical symptoms are unidentifiable.

1 | INTRODUCTION

Chronic or recurrent back pain in the paediatric population is less prevalent than adults, affecting 14–24% of children and adolescents and is usually associated with post-trauma or known severe pathological conditions (Altaf et al., 2014; Balague et al., 1999; Davis & Williams, 2008; Haidar et al., 2011; Moreno, 2017). However, when pathoanatomical symptoms are unidentifiable, the diagnosis is labelled as non-specific chronic back pain. Patients with chronic back pain experience functional disability, higher rates of missed school, poor sleep quality and mental health problems when compared to age-matched pain-free controls (Balagué et al., 1995; Huguet & Miro, 2008; O'Sullivan et al., 2011; Watson et al., 2002; Wojtowicz & Banez, 2015), and are at risk of experiencing chronic pain throughout adulthood (Brattberg, 2004; Hestbaek et al., 1976; Jeffries et al., 2007; Mikkelsen et al., 2008).

A major limitation in treatment outcomes for chronic back pain is the heterogeneity of the population. Moreover, there are limited paediatric studies, especially randomized control trials, that have documented standardized measures associated with treatment response (McGrath et al., 2008; Randall et al., 2018; Simons et al., 2018). We have previously shown that different pain processing mechanisms may be involved in adolescents with idiopathic scoliosis and chronic back pain (Teles et al., 2019). These results highlight that despite the similar diagnosis, characterizing the psychophysical profile of patients with chronic pain through quantitative sensory tests (QST) may be relevant to consider as a component to guide pain management to become tailored to address underlying etiological mechanisms.

Due to the heterogeneity within chronic pain conditions and that different chronic pain conditions may share similar characteristics (Diatchenko et al., 2006), researchers and clinicians have turned to identifying subgroups with distinct psychophysical profiles in different samples of patients with chronic pain. Subgroups of adult patients with chronic low back pain (Coronado et al., 2014; Rabey et al., 2015), temporomandibular disorder (Bair et al., 2016) and other chronic pain conditions (Baron et al., 2017) have been successfully identified. Rabey et al. (2015) investigated subgroups in a cohort of chronic low back pain based on their QST results. They identified three clusters in which those that displayed increased thermal

and pressure pain sensitivity had a greater proportion of females, and higher scores for depression and poor sleep quality (Rabey et al., 2015). The main limitation of this study was including only the QST results as factors in their cluster analysis. Numerous factors influence quantitative sensory testing, such as age, sex and psychosocial factors (Blankenburg et al., 2010; Cornelissen et al., 2014; Hirschfeld et al., 2012; Rolke et al., 2006). Including these factors within the cluster analysis may give more insight into data interpretation and interventions tailored for these subgroups. Bair et al. (2016) included psychophysical and psychosocial measures in their cluster analysis. However, they used a supervised cluster approach which involves selecting specific variables in their analysis aligning with their objective to identify risk factors for chronic pain in healthy individuals who have a similar psychophysical profile as patients with temporomandibular disorders (Bair et al., 2016).

Researchers and clinicians have also turned to identify heterogeneous subgroups of paediatric chronic pain patients (Scharff et al., 2005; Schurman et al., 2008; Wager et al., 2014; Walker et al., 2012). However, these studies strictly investigated pain and psychosocial characteristics in their cluster analysis and there are limited data evaluating subgroups based on the psychophysical profile of paediatric chronic pain patients. Therefore, the objective of this study was to identify specific psychophysical and psychosocial profiles among a cohort of paediatric patients with chronic back pain. The aim was to conduct an unsupervised statistical clustering approach involving the QST results and psychosocial context of the patients. We hypothesized that subgroups of patients with chronic back pain can be clustered based on similar psychophysical and psychosocial characteristics.

2 | Methods

2.1 | Study approval

Ethics approval was obtained prior to the beginning of the recruitment from the Research Ethics Board of McGill University (A11-M62-15B). Participants received written informed consent prior to inclusion in the study and a signature was obtained by the participant or their parent/legal guardian, if the participant was under the age of 14 years old, prior to the beginning of the study. The

study was conducted in accordance with the Declaration of Helsinki. All participants were de-identified according to the institutional ethics guidelines.

2.2 | Participants

Patient recruitment occurred between January 2016 and October 2017. Potential participants from the spine and orthopaedic outpatient clinics and the Chronic Pain Services of our institution were identified by a research assistant based on the presence of chronic pain reported in their electronic medical charts or by reference of the patient's physician. At their hospital visit for treatment-seeking either for an orthopaedic condition or for pain itself, patients were approached by a research assistant to participate in the study and to confirm eligibility criteria prior to receiving signed consent. Inclusion criteria were being aged between 10 and 21 years old with chronic back pain (persistent or recurrent pain at least once a week for longer than three months) (Treede et al., 2019). Patients who did not speak English or French or had a diagnosis of developmental delay that would interfere with completing measures were excluded.

2.3 | Primary outcome measures

2.3.1 | Sociodemographic characteristics and medical history

Patient characteristics such as age, sex, ethnicity and pathology were collected by a research assistant.

2.3.2 | Clinical characteristics

Pain assessment was mainly conducted in the form of a face-to-face interview and with the use of standardized pain-related questionnaires that have been validated in clinical paediatric studies assessing pain (Claar & Walker, 2006; David et al., 2015; Palermo, 2009; Siu et al., 2012). Patients were asked about the duration and frequency of their pain. The location of pain was reported using a modified version of the adolescent paediatric pain tool (APPT) (Fernandes et al., 2014), in which a diagram of the back was divided into 10 segments to identify specific pain locations (Savedra et al., 1989; Teles et al., 2019). In addition, pain intensity experienced over the last month in each divided back segment of the diagram was reported using an 11-point numerical rating scale (NRS 0–10, 0 = no pain, 10 = the worst pain imaginable). Moreover, the pain experience was assessed using a list of 67 descriptive

words in the APPT, assessing the four dimensions of pain (sensory, affective, evaluative and temporal) (Savedra et al., 1993). The APPT has been shown to have adequate content, construct, and criterion validity and reliability in clinical and non-clinical groups of children and adolescents between 8 and 17 years old (Jacob et al., 2014). To identify if their pain had a neuropathic component, the Douleur Neuropathique 4 (DN4) questionnaire was completed by patients. By summing all 10 questions, scores equal to or greater than 4 indicated that the pain experienced by the patient is likely neuropathic (Bouhassira et al., 2005; David et al., 2015). The DN4 questionnaire has not been validated in children and adolescents. However, despite its very low-level evidence for satisfactory criterion validity and low-level evidence for satisfactory construct validity and reliability, the DN4 questionnaire has been described to be the most suitable for clinical use (de Leeuw et al., 2020; Mathieson et al., 2015).

2.3.3 | Anxiety and depressive symptoms

The revised child anxiety and depression scale (RCADS) questionnaire was completed by patients to assess children's self-report of depression and anxiety corresponding to the 4th edition of the diagnostic and statistical manual of mental disorders (Chorpita et al., 2000). Based on the patient's age and grade in school, their total scores are converted into a T-score, in which a T-score between 65 and 69 indicates borderline clinical threshold, and a T-score of 70 or higher indicates above clinical threshold for anxiety and depression. The RCADS has been validated in clinical and non-clinical groups of children and adolescents in grades 3–12 and showed good internal consistency (Cronbach $\alpha = 0.78$ – 0.88) and item set and factor definitions consistent with DSM-IV anxiety disorders and depression (Chorpita et al., 2000, 2005).

2.3.4 | Functional disability

The functional disability inventory (FDI) questionnaire was completed by patients, in which the total score is summed to detect different levels of disability (Walker & Greene, 1991). The FDI has been reported to have high internal consistency, moderate to high test-retest reliability, moderate cross-informant (parent-child) reliability and good predictive validity (Claar & Walker, 2006; Walker & Greene, 1991). The FDI is based on four-level classifications system: A score of 0 to 12 inclusively represents no/minimal disability and patients can function well, despite experiencing pain; a score from 13 to 20 inclusively represents mild disability; a score from 21 to 29 inclusively

represents moderate disability; a score of 30 or higher represents severe disability.

2.3.5 | Sleep quality

The Pittsburgh sleep quality index (PSQI) questionnaire was completed by patients to assess sleep quality, in which a global score of 5 or higher indicated poor sleep quality (Buysse et al., 1989). The PSQI is the most commonly used measure in clinical and research settings showing good internal consistency (Cronbach $\alpha = 0.70$ – 0.83) and has been validated in clinical and non-clinical groups of adolescents (Larche et al., 2021; Mollayeva et al., 2016; Raniti et al., 2018).

2.3.6 | Quantitative sensory testing

Each patient underwent a specific protocol of mechanical and thermal quantitative sensory tests (QST) to obtain a comprehensive profile of somatosensory functioning. The protocol was based on an initiative of the Quebec Pain Research Network (Ferland et al., 2018a, 2018b). All tests were conducted by research assistants who were trained and evaluated by the principal investigator of the study. Mechanical and thermal procedures were performed on the left volar forearm, 2 inches from the left elbow crease as the control area and followed by the most painful anatomical region of the back indicated by the patient as the affected area. A demonstration of every test was explained and performed on the left thenar eminence of the patient. The protocol previously described (Teles et al., 2019) consisted of four tests assessing six parameters: Mechanical detection threshold, pressure pain threshold, heat pain threshold, heat tolerance threshold, temporal summation of pain and conditioned pain modulation.

Mechanical quantitative sensory testing assessment

Mechanical detection threshold (MDT), using standardized von Frey filaments (Touch-Test™ Sensory Evaluators, USA) with forces ranging between 0.008 and 300 grams, was evaluated to assess tactile sensitivity (Blankenburg et al., 2010; Teles et al., 2019; Thibault et al., 1994). The geometric mean of six threshold values was calculated and reported in grams. Pressure pain threshold (PPT), using the JTech Algometer (JTech Medical, USA) with a 1-cm² probe, was evaluated to assess deep-tissue sensitivity (Blankenburg et al., 2010; Teles et al., 2019). The pressure was applied increasing at a rate of ~1 N/s (~10 kPa/s) until the patient reported pain. The mean of three recorded values was calculated and reported in Newtons.

Thermal quantitative sensory testing assessment

Heat pain threshold (HPT) and heat pain tolerance threshold (HTT) was evaluated using a 9-cm² warm calibrated thermode connected to the Q-sense apparatus (Medoc, Israel). The thermode, initially set at 32.0°C, was placed on the left volar forearm of the patient and increased at a rate of 0.3°C/second to reach the maximum value of 50.0°C as a security cut-off. HPT (when the patient first report pain) and HTT (when the pain was intolerable) were assessed three times and the mean was calculated and reported in degree Celsius.

A conditioned pain modulation (CPM) paradigm was then performed using tonic heat on the right forearm as the test stimulus and the cold pressor task on the left arm as the conditioning stimulus as previously described protocols (Ferland et al., 2018a, 2018b; Potvin & Marchand, 2016; Teles et al., 2019). First, a thermode was applied to the forearm to reach a pre-determined test temperature to a 5/10 pain intensity. Once the target temperature was reached, it remained constant for 120 seconds. Patients were not told that the temperature of the thermode would remain constant over time to avoid expectation effects. Using a computerized pain scale (CoPS 0–10; 0 = no pain, 10 = the worst pain imaginable), patients were asked to continuously rate their pain to identify if there is temporal summation of pain (TSP) (Ferland et al., 2018a, 2018b; Teles et al., 2019). The presence of temporal summation (i.e. endogenous facilitatory pain response) was defined as a 2/10 increase in pain intensity using the CoPS at the end of the test in comparison to the pain intensity 60 s after the beginning of the test. A change in pain intensity of 2/10 on a NRS was determined as a minimum clinically significant difference (Farrar et al., 2001). Once the tonic heat test was completed, patients performed a cold pressor task (CPT) involving the immersion of their forearm in a filled with cold water (12°C) for 2 min to trigger the descending inhibitory pain response. The CPT was immediately followed by a second tonic heat test. The patient's capacity to endogenously inhibit pain was described previously as the diffuse noxious inhibitory control, and here measured as the CPM efficiency was then calculated as the percentage difference between the mean pain intensity of the test stimulus before and after the conditioning stimulus over the mean pain intensity during the test stimulus before the conditioning stimulus. A negative percentage result under –30% indicated an optimal inhibitory pain response, a negative percentage result between –10 and –30% indicated a suboptimal inhibitory pain response, and a negative percentage result above –10% or a positive percentage result indicated an inefficient or facilitatory pain response (Ferland et al., 2018a, 2018b; Teles et al., 2019). A 10%–30% reduction in pain was labelled to be a minimal improvement, whilst a 30% reduction in

pain intensity was labelled to be a clinically important difference in pain intensity (Farrar et al., 2001) and is approximately the mean value of inhibitory CPM observed in previous studies (Ferland et al., 2018a, 2018b; Potvin & Marchand, 2016; Teles et al., 2019; Tousignant-Laflamme et al., 2008).

2.4 | Statistical analysis

Descriptive statistics were performed using the R Studio software to summarize the collected data regarding the patients' characteristics, clinical data relative to pain, psychosocial factors and QST results. Sample size requirements for principal component analysis (PCA) are not definitive and are dependent on many factors. Therefore, the sample size was based on population proportion in which minimally 14% of the paediatric population is affected by chronic back pain. Based on this assumption, a sample size of 185 patients is required to achieve 90% statistical power at the 0.05 significance level.

An unsupervised cluster analysis was performed using the FactoMineR package in the R Studio software (Le et al., 2008) to subgroup patients into clinical profiles and potentially identify responders to specific therapeutic strategies. To profile the patients based on their psychophysical and psychosocial characteristics, the cluster analysis involved 17 indicator variables: sensory descriptors, affective descriptors, evaluative descriptors, temporal descriptors, DN4 total score, FDI total score, RCADS total T-score, PQSI global score, mechanical detection threshold in the control and affected area, pressure pain threshold in the control and affected area, heat pain threshold, heat tolerance threshold, the average pain score during the cold pressor task, CPM efficiency score and the pain score during the thermal temporal summation of pain. Other quantitative and qualitative outcome measures were included as supplementary variables as they do not represent underlying mechanisms of pain and instead may represent consequences of chronic back pain: location of recruitment, age, sex, ethnicity, duration of pain, frequency of pain, duration of painful episodes, pathology, most painful location, average pain reported in the back, pain radiating down the legs and test temperature for the CPM assessment. Since all measures had different units, iterative PCA using the FactorMineR package in the R Studio software was first conducted as a data reduction technique standardizing all variables into Z-scores. Principal component analysis was conducted to investigate interrelationships between and within psychophysical and psychosocial variables to determine whether a smaller number of principal components is representative of the total variation in the data. Standardization of all

variables was to ensure equal importance of each variable in the PCA. Missing data for a maximum of two variables were observed for eight patients. No differences were observed in these eight patients in comparison to the rest of the sample regarding their demographic characteristics (data not shown). Therefore, these eight patients were kept in the analysis. Missing data were imputed for the indicator variables using the missMDA package which takes into account similarities between the values of the variables of each patient (Josse & Husson, 2016; Le et al., 2008). Principal components (PCs) with eigenvalues >1 were retained (Hair, 2010). Variable loading on each principal component was considered significant if >0.3 (Hair, 2010). Hierarchical clustering with k-means consolidation was conducted on the principle components. The hierarchical clustering was, therefore, performed multiple times to minimize within-cluster variability and maximize between-cluster variability. The best partition of clusters was the one with the highest relative loss of inertia (Hair, 2010). An analysis of variance (ANOVA) model was conducted along with a Fisher test to determine which principal components best represent each cluster and determine cluster effect. Differences between clusters regarding their characteristics, clinical data relative to pain, psychosocial factors and QST results was conducted using the chi-squared test and Kruskal-Wallis one-way ANOVA followed by Dunn's test depending on whether the variable was qualitative or quantitative, respectively.

3 | RESULTS

Two hundred and four patients were recruited for this cross-sectional study. However, six patients dropped out prior to the quantitative sensory tests. Therefore, the data of 198 patients with chronic back pain were analysed, in which 170 (85.9%) were recruited from the spine and orthopaedic outpatient clinics whilst 28 (14.1%) the chronic pain services of our institution. The mean age was 15.69 ± 2.25 years old and 81.8% of our cohort were females (Table 1). The majority of the patients were Caucasian (90.4%), experience pain for more than 12 months (72.2%), experience pain on a daily basis (65.2%) and experience constant painful episodes (55.6%). Moreover, 25.8% of the cohort reported back pain radiating down their legs, whilst 27.8% of our cohort self-report their pain as most likely to be neuropathic. Among the cohort, 71.2% reported their most painful location along their spine. Furthermore, 54.6% of the cohort self-reported mild to severe functional disability, 7.6% self-reported borderline of above clinical threshold symptoms of anxiety and depression and 72.7% self-reported poor sleep quality. Large variability was observed for the QST results in the cohort. The inhibitory

TABLE 1 Demographics, clinical data relative to pain and psychosocial and psychophysical characteristics of cohort

Variable	Total sample (n = 198)
Location of recruitment, n (%)	
Spine and orthopaedic outpatient clinics	170 (85.9)
Chronic pain services	28 (14.1)
Age, Mean \pm SD	15.69 \pm 2.25
Sex, n (%)	
Female	162 (81.8)
Male	36 (18.2)
Ethnicity, n (%)	
Caucasian	179 (90.4)
Black or African American	10 (5.1)
Asian	4 (2.0)
Interracial	5 (2.5)
Duration of pain, n (%)	
3–6 months	14 (7.1)
6–12 months	41 (20.7)
> 12 months	143 (72.2)
Frequency of pain, n (%)	
Daily	129 (65.2)
Every 2nd day	43 (21.7)
Once a week	26 (13.1)
Duration of painful episodes, n (%)	
Few seconds	8 (4.0)
Few minutes	36 (18.2)
One hour	44 (22.2)
Constant	110 (55.6)
Pathology, n (%)	
Arthritic	6 (3.0)
Disc protrusion	8 (4.0)
Mechanical back pain	14 (7.1)
Scoliosis	115 (58.1)
Spondylolysis/Spondylolisthesis	13 (6.6)
Tight hamstrings	9 (4.5)
Non-specific back pain	33 (16.7)
Most painful location, n (%)	
Neck	3 (1.5)
Left upper back	6 (3.0)
Center upper back	38 (19.2)
Right upper back	11 (5.6)
Left middle back	8 (4.0)
Center middle back	37 (18.7)
Right middle back	12 (6.1)
Left lower back	12 (6.1)

TABLE 1 (Continued)

Variable	Total sample (n = 198)
Center lower back	63 (31.8)
Right lower back	6 (3.0)
Average pain reported, NRS (0–10), Mean (CI)	
Neck	2.91 (2.50–3.32)
Left upper back	2.73 (2.32–3.14)
Center upper back	3.44 (3.00–3.87)
Right upper back	2.46 (2.05–2.87)
Left middle back	2.80 (2.39–3.21)
Center middle back	4.32 (3.90–4.74)
Right middle back	2.56 (2.16–2.95)
Left lower back	3.07 (2.61–3.53)
Center lower back	4.09 (3.63–4.54)
Right lower back	3.18 (2.73–3.64)
Pain radiating down legs, n (%)	
Yes	51 (25.8)
No	140 (70.7)
Descriptors of pain used, Mean (%) \pm SD	
Sensory	18.04 \pm 11.61
Affective	8.92 \pm 12.00
Evaluative	34.13 \pm 21.41
Temporal	23.94 \pm 13.78
Neuropathic component, n (%)	
Mean score of DN4 questionnaire, Mean \pm SD	2.46 \pm 2.08
Likely neuropathic	55 (27.8)
Not likely neuropathic	143 (72.2)
Functional Disability, n (%)	
Mean score of FDI, Mean \pm SD	15.43 \pm 10.31
None or minimal	89 (44.9)
Mild	50 (25.3)
Moderate	37 (18.7)
Severe	21 (10.6)
Anxiety and Depression Symptoms, n (%)	
Mean T-score of RCADS, Mean \pm SD	45.34 \pm 12.39
Below clinical threshold	183 (92.4)
Borderline	5 (2.5)
Above clinical threshold	10 (5.1)
Sleep Quality, n (%)	
Mean global score of PSQI, Mean \pm SD	6.98 \pm 3.48
Good sleep quality	54 (27.3)
Poor sleep quality	144 (72.7)
MDT (g), Mean \pm SD	

TABLE 1 (Continued)

Variable	Total sample (n = 198)
Control area	0.52 ± 1.65
Affected area	1.47 ± 12.37
PPT (N), Mean ± SD	
Control area	27.62 ± 14.82
Affected area	26.38 ± 17.44
HPT (°C), Mean ± SD	39.24 ± 3.17
HTT (°C), Mean ± SD	45.16 ± 2.41
Test temperature for CPM assessment (°C), Mean ±SD	43.56 ± 2.51
CPT average pain score NRS (0–10), Mean ± SD	6.98 ± 2.32
CPM, n (%)	
CPM efficiency (%), Mean ±SD	−29.44 ± 42.87
Inefficient	51 (25.8)
Suboptimal	45 (22.7)
Optimal	102 (51.5)
TSP, n (%)	
TSP pain score NRS (0–10), Mean ±SD	0.09 ± 2.07
No presence	171 (86.4)
Presence	27 (13.6)

Abbreviations: CI, 95% confidence interval; CPM, conditioned pain modulation; CPT, cold pressor task; DN4, douleur neuropathique 4 questionnaire; FDI, functional disability index; HPT, heat pain threshold; HTT, heat tolerance threshold; MDT, mechanical detection threshold; PPT, pressure pain threshold; PSQI, Pittsburgh sleep quality index; RCADS, revised children's anxiety and depression scale; SD, standard deviation; TSP, temporal summation of pain.

pain control assessment revealed great variability among the cohort. The CPM efficiency was optimal in 51.5%, sub-optimal in 22.7% and inefficient in 25.8% of the cohort. Moreover, 13.6% of the cohort displayed temporal summation of pain.

3.1 | Principal component analysis

Iterative principal component analysis derived five principal components (PC) with eigenvalues >1 accounting for 59.2% of the total variation in the data. Variable loading on each principal component is summarized in Table 2. The PCs can be summarized as representing the dimensions of psychosocial factors (PC1), pressure pain and heat tolerance thresholds (PC2), mechanical detection threshold (PC4) and CPM efficiency (PC5). No significant variable loading was observed for PC3. The PC scores were calculated for each patient using the component loadings and were used to replace the indicator variables in the cluster analysis.

3.2 | Cluster analysis

Hierarchical clustering partitioned our patients into three clusters accounting for 34.73% of the total variation in the data. Eighty-nine patients (44.9%) were grouped in cluster 1, 71 patients (35.9%) and 38 patients (19.2%) were grouped in cluster 2 and cluster 3, respectively. Figure 1 displays the three clusters according to principal components 1 and 2. Patients grouped in cluster 1 are characterized by significantly low values for PC1 ($t = 5.77$, $p < 0.001$) and high values for PC2 ($t = 5.43$, $p < 0.001$) and we, therefore, named it the adaptive cluster. In contrast, patients grouped in cluster 2 are mainly characterized by significantly low values for PC2 ($t = 7.54$, $p < 0.001$) and was, therefore, named the pain-sensitive cluster. Moreover, patients grouped in cluster 3 are mainly characterized by significantly high values for PC1 ($t = 11.54$, $p < 0.001$) and thus named the high somatic symptoms cluster.

3.3 | Profiling of clusters

No significant differences were observed between clusters in regard to their age, sex, ethnicity, duration of pain, duration of painful episodes, pathology or location of pain (Table 3). However, a significant association was observed between cluster membership and the location of recruitment in the study ($p < 0.001$) and the reported frequency of pain ($p = 0.008$). A higher proportion of patients grouped in the high symptomatic symptoms cluster were recruited from the chronic pain services at our institution and all reported pain at least every second day. Moreover, the high somatic symptom cluster reported significantly higher pain intensity in all regions of the back ($p < 0.05$). Furthermore, a higher proportion of patients in the high somatic symptoms clusters reported their back pain radiating down their legs ($p < 0.001$).

Figure 2 displays the Z-scores for the indicator variables for the respective three clusters. Significant between-cluster differences in regard to the raw data of the indicator variables were observed (Table 4). The high somatic symptoms cluster was characterized to significantly have the highest scores for all the questionnaires completed ($p < 0.001$). The high somatic symptoms cluster were characterized to group patients who used more sensory, affective, evaluative and temporal descriptors of pain, more likely reported their pain as neuropathic of nature, reported more functional disability, reported symptoms of anxiety and depression, and reported poor sleep quality. The adaptive cluster, in comparison to the pain-sensitive and high somatic symptoms clusters, was characterized to significantly have the highest pressure pain threshold in the control and affected area, highest

TABLE 2 Principal component analysis of psychophysical variables

Variable	Component 1	Component 2	Component 3	Component 4	Component 5
Sensory descriptors	0.556	0.115	0.054	0.007	0.003
Affective descriptors	0.463	0.053	0.017	0.050	0.008
Evaluative descriptors	0.445	0.022	0.103	0.001	0.009
Temporal descriptors	0.188	0.071	0.144	0.012	0.005
DN4 Total score	0.321	0.080	0.004	0.074	0.058
FDI Total score	0.521	0.058	0.048	0.008	0.005
Anxiety and Depression Total T-score	0.303	0.003	0.169	0.075	0.005
PSQI score	0.295	0.054	0.209	0.037	0.020
MDT control	0.005	0.016	0.001	0.496	0.008
MDT affected	0.016	0.003	0.069	0.115	0.377
PPT control	0.140	0.401	0.121	0.036	0.007
PPT affected	0.136	0.319	0.202	0.090	0.000
HPT	0.142	0.289	0.072	0.039	0.007
HTT	0.164	0.446	0.116	0.015	0.006
CPT average pain score	0.130	0.259	0.012	0.000	0.181
CPM efficiency	0.003	0.050	0.002	0.156	0.451
TSP pain score	0.002	0.136	0.122	0.008	0.185

Note: Variable loading on each component was considered significant if >0.3 (bolded).

Abbreviations: CPM, conditioned pain modulation; CPT, cold pressor task; DN4, douleur neuropathique 4 questionnaire; FDI, functional disability index; HPT, heat pain threshold; HTT, heat tolerance threshold; MDT, mechanical detection threshold; PPT, pressure pain threshold; PSQI, Pittsburgh sleep quality index; TSP, temporal summation of pain.

heat pain and tolerance threshold, and lowest pain intensity reported during the cold pressor task ($p < 0.001$). Interestingly, patients in the adaptive cluster had a higher proportion of patients that display temporal summation pain than the pain-sensitive cluster and the high somatic symptoms cluster ($p = 0.005$). The pain-sensitive cluster, in general, displayed lower pressure pain threshold in the control and affected area, lower heat pain and tolerance threshold, and higher pain intensity reported during the cold pressor task than the adaptive cluster ($p < 0.001$), but also displayed lower scores for all the questionnaires completed than the high somatic symptoms cluster ($p < 0.001$).

4 | DISCUSSION

The objective of this study was to identify specific psychophysical and psychosocial profiles among a cohort of paediatric patients with chronic back pain. A cluster analysis of these patients suggested three subgroups and were best described by two principal components representing the dimensions of psychosocial factors, and pressure pain and heat tolerance thresholds. Cluster membership did not vary significantly by age,

sex, ethnicity, duration of pain, duration of painful episodes, pathology or most painful location as observed by Schurman et al. (2008) in a cluster analysis of children with recurrent abdominal pain (Schurman et al., 2008). Furthermore, no difference in tactile sensitivity or efficiency of their descending inhibitory pain response was observed among the groups. To our knowledge, this is the first cluster analysis performed with youth experiencing chronic back pain. Furthermore, our cluster model included QST results and psychosocial factors, building on prior work by Rabey et al. (2015) and Baron et al. (2017) who included only QST results in their cluster analysis (Baron et al., 2017; Rabey et al., 2015), and adult and paediatric studies who based their analysis on pain descriptors and psychological symptoms (Larsson et al., 2017; Scharff et al., 2005; Schurman et al., 2008; Wager et al., 2014). Moreover, we conducted an unsupervised approach to cluster analysis, unlike Bair et al. (2016) who conducted a supervised cluster analysis to determine risk factors for temporomandibular disorder in healthy individuals. Our unsupervised approach was appropriate for the cross-sectional design of the study to identify clusters of patients with chronic back pain that may benefit from a tailored management based on their psychophysical and psychosocial profiles.

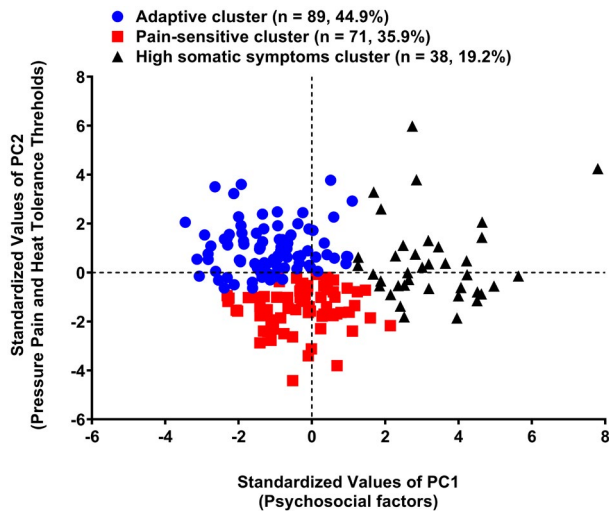


FIGURE 1 Results of the hierarchical clustering analysis displaying three clusters derived from the principal component (PC) scores of PC1 and PC2 representing the dimensions of psychosocial factors, and pressure pain and heat tolerance thresholds, respectively. The adaptive cluster is characterized by significantly higher values for pressure pain and heat tolerance thresholds. In contrast, the pain-sensitive cluster is mainly characterized by lower values for pressure pain and heat tolerance thresholds. The high somatic symptoms cluster is mainly characterized by having the highest values for the dimension of psychological factors

4.1 | Profiling of clusters

The adaptive cluster represented 44.9% of the patients and was characterized by a higher thermal and pressure pain threshold. Subgroups of adult patients with chronic back pain presenting with similar psychophysical characteristics have been identified (Coronado et al., 2014; Rabey et al., 2015). However, the meaning of the low pressure and heat sensitivity in our cohort remains unclear. The results of sensory testing of the patients in this cluster are visually similar to reference values established in the hand and foot in the paediatric population (Blankenburg et al., 2010). This is unlike other paediatric population-based studies that show lower pressure pain thresholds in adolescents with chronic pain (Tham et al., 2016). However, Tham et al. (2016) has shown in a large cohort of adolescents that the heat pain threshold and cold pressor data were not significantly different between those with and without chronic pain (Tham et al., 2016). Contrarily to Tham et al., Sethna et al. (2007) observed in paediatric patients with complex regional pain syndromes, an overall significant difference with healthy controls for cold and heat pain thresholds. However, a large percentage of patients were within normal reference intervals (Sethna et al., 2007). Our results highlight that despite the presence of chronic back pain, there is a subgroup of patients

that do not display deep tissue sensitivity or thermal hyperalgesia in either the affected or control area of the body.

A larger proportion of patients that displayed the presence of thermal temporal summation of pain were found in the adaptive cluster. In a systematic review in children with chronic pain conducted by Pas et al. (2018), central hyperexcitability was shown to be present in several paediatric chronic pain conditions (Pas et al., 2018). Therefore, the sensitization to a tonic noxious heat stimulation in a region of the body remote from the primary area of pain may suggest that the chronic pain of the patients in the adaptive cluster arise or persist from central processes (Giesecke et al., 2004). In a systematic review on adult patients conducted by Hubscher et al. (2013), a fair association between spinal pain intensity and thermal temporal summation was observed (Hubscher et al., 2013). Although we did not conduct this analysis in our cohort, altogether, our results may suggest that the persistent back pain in the adaptive cluster may arise from central facilitation.

The pain-sensitive cluster, representing 35.9% of the cohort was characterized to have lower thermal and pressure pain thresholds in comparison to the adaptive cluster. Lower pain thresholds in the affected region of the body have been observed in other chronic pain conditions in paediatrics (Cornelissen et al., 2014; Tham et al., 2016). We recently observed (Teles et al., 2019) in a subset of the cohort with idiopathic scoliosis with chronic back pain that the severity of their curve was significantly associated with deep tissue sensitivity in the back (Teles et al., 2019). Therefore, the diagnosis that may underlie that chronic back pain should not be ignored in this subgroup. Studies investigating strictly psychophysical profiles of adult chronic pain patients observe minimally a three-group solution (Baron et al., 2012; Rabey et al., 2015), unlike our results revealing two psychophysical profiles. However, our results highlight that, in contrast to the adaptive cluster, there is a subgroup of patients that display maladaptive pain mechanisms suggesting possible involvement of central and peripheral pain mechanisms that can be targeted.

The adaptive cluster and the pain-sensitive cluster were characterized to have lower scores for all questionnaires (i.e. use less descriptors of pain, not likely to report their pain as neuropathic in nature, none to mild functional disability, report less anxiety and depression symptoms below the clinical threshold and report better sleep quality). Similarly, to other studies conducting cluster analysis of psychological profiles among children with chronic pain, at least two subgroups can be observed (Scharff et al., 2005; Schurman et al., 2008). Scharff et al. (2005) observed in a subgroup of children with chronic pain (52.1%) whose questionnaire scores fell within established population

TABLE 3 Differences between clusters regarding demographics and clinical data relative to pain

Variable	Adaptive cluster (n = 89)	Pain-sensitive cluster (n = 71)	High somatic symptoms cluster (n = 38)	χ^2 value	p-value
Location of recruitment, n (%)					
Spine and orthopaedic outpatient clinics	83 (93.3)	62 (87.3)	25 (65.8)	16.75*	<0.001
Chronic pain services	6 (6.7)	9 (12.7)	13 (34.2)		
Age, Mean \pm SD	15.74 \pm 2.15	15.32 \pm 2.34	16.26 \pm 2.25	2.23 [†]	0.110
Sex, n (%)					
Female	69 (77.5)	61 (85.9)	32 (84.2)	2.05*	0.359
Male	20 (22.5)	10 (14.1)	6 (15.8)		
Ethnicity, n (%)					
Caucasian	82 (92.1)	60 (84.5)	37 (97.4)	11.00*	0.088
Black or African American	2 (2.2)	8 (11.3)	0 (0.0)		
Asian	3 (3.4)	1 (1.4)	0 (0.0)		
Interracial	2 (2.2)	2 (2.8)	1 (2.6)		
Duration of pain, n (%)					
3–6 months	7 (7.9)	6 (8.5)	1 (2.6)	1.91*	0.751
6–12 months	20 (22.5)	14 (19.7)	7 (18.4)		
> 12 months	62 (69.7)	51 (71.8)	30 (78.9)		
Frequency of pain, n (%)					
Daily	55 (61.8)	40 (56.3)	34 (89.5)	13.71*	0.008
Every 2nd day	20 (22.5)	19 (26.8)	4 (10.5)		
Once a week	14 (15.7)	12 (16.9)	0 (0.0)		
Duration of painful episodes, n (%)					
Few seconds	6 (6.7)	2 (2.8)	0 (0.0)	7.78*	0.255
Few minutes	16 (18.0)	16 (22.5)	4 (10.5)		
One hour	20 (22.5)	17 (23.9)	7 (18.4)		
Constant	47 (52.9)	36 (50.7)	27 (71.1)		
Pathology, n (%)					
Arthritic	3 (3.4)	1 (1.4)	2 (5.3)	16.48*	0.170
Disc protrusion	4 (4.5)	1 (1.4)	3 (7.9)		
Mechanical back pain	9 (10.1)	3 (4.2)	2 (5.3)		
Scoliosis	52 (58.4)	47 (66.2)	16 (42.1)		
Spondylolysis/Spondylolisthesis	7 (7.9)	5 (7.0)	1 (2.6)		
Tight hamstrings	4 (4.5)	3 (4.3)	2 (5.3)		
Non-specific back pain	10 (11.2)	11 (15.5)	12 (31.6)		
Most painful location, n (%)					
Neck	2 (2.2)	0	1 (2.6)	17.10*	0.516
Left upper back	2 (2.2)	1 (1.4)	3 (7.9)		
Center upper back	13 (14.6)	15 (21.1)	10 (26.3)		
Right upper back	5 (5.6)	5 (7.0)	1 (2.6)		
Left middle back	5 (5.6)	3 (4.3)	0		
Center middle back	15 (16.9)	14 (19.7)	8 (21.1)		
Right middle back	6 (6.7)	5 (7.0)	1 (2.6)		
Left lower back	6 (6.7)	6 (8.5)	0		
Center lower back	32 (36.0)	20 (28.2)	11 (28.9)		

TABLE 3 (Continued)

Variable	Adaptive cluster (n = 89)	Pain-sensitive cluster (n = 71)	High somatic symptoms cluster (n = 38)	χ^2 value	p-value
Right lower back	3 (3.4)	1 (1.4)	2 (5.3)		
Average pain reported, NRS (0–10), Mean (CI)					
Neck	2.82 (2.22–3.42) ^c	2.28 (1.65–2.90) ^c	4.29 (3.21–5.37) ^{a,b}	10.84 [†]	0.004
Left upper back	2.30 (1.75–2.85) ^c	2.19 (1.58–2.81) ^c	4.75 (3.61–5.89) ^{a,b}	17.51 [†]	<0.001
Center upper back	2.89 (2.29–3.48) ^c	3.32 (2.58–4.07) ^c	4.93 (3.87–6.00) ^{a,b}	10.63 [†]	0.005
Right upper back	2.08 (1.52–2.65) ^c	1.99 (1.37–2.60) ^c	4.22 (3.10–5.35) ^{a,b}	14.40 [†]	<0.001
Left middle back	2.43 (1.86–3.00) ^c	2.56 (1.88–3.24) ^c	4.11 (3.03–5.19) ^{a,b}	8.58 [†]	0.014
Center middle back	3.87 (3.26–4.47) ^c	4.27 (3.55–4.99)	5.47 (4.53–6.42) ^a	7.68 [†]	0.021
Right middle back	2.15 (1.57–2.74) ^c	2.49 (1.87–3.11)	3.63 (2.60–4.66) ^a	7.64 [†]	0.022
Left lower back	2.65 (1.99–3.31) ^c	2.83 (2.09–3.57) ^c	4.50 (3.33–5.67) ^{a,b}	10.04 [†]	0.007
Center lower back	3.70 (3.06–4.33) ^c	3.65 (2.86–4.44) ^c	5.82 (4.77–6.87) ^{a,b}	13.54 [†]	0.001
Right lower back	2.37 (1.74–3.00) ^c	3.08 (2.36–3.81) ^c	5.28 (4.19–6.37) ^{a,b}	19.97 [†]	<0.001
Pain radiating down legs, n (%)					
Yes	18 (20.2)	14 (19.7)	19 (50.0)	18.00*	<0.001
No	70 (78.7)	55 (77.5)	15 (39.5)		

Note: p-values ≤ 0.05 are bolded.

Abbreviations: CI, 95% confidence interval; SD, standard deviation.

^aSignificant difference with cluster 1.

^bSignificant difference with cluster 2.

^cSignificant difference with cluster 3.

*Chi-squared test statistic.

[†]Kruskal-Wallis one-way analysis of variance chi-squared test statistic.

norms and was distinguished by low levels of disability (Scharff et al., 2005). Schurman et al. (2008) conducted a similar cluster analysis and also observed more than half of their sample with better psychological functioning (Schurman et al., 2008). Therefore, our results are consistent with the chronic pain model where inter-individual variability in the relative contributions of multiple elements of pain would be expected.

Despite their low thermal and pressure pain threshold similar to the pain-sensitive cluster, the high somatic symptoms cluster, representing 19.2% of patients, displayed higher self-report of pain intensity in the back, functional disability, anxiety and depression symptoms, and poor sleep quality. This is as observed by other research groups investigating variations in psychosocial profiles in children and adolescents with chronic pain (Scharff et al., 2005; Schurman et al., 2008). Functional disability, mental distress and sleep problems have been shown to be associated with pain in the paediatric population (Eccleston et al., 2004; Lewandowski Holley et al., 2017; Long et al., 2008; Wojtowicz & Banez, 2015). However, the cause-and-effect relationship between pain and these outcomes is unclear. Furthermore, studies investigating strictly psychosocial subgroups of paediatric chronic pain patients

observe minimally a three-group solution (Scharff et al., 2005; Schurman et al., 2008; Wager et al., 2014), unlike our results revealing two psychosocial profiles. Therefore, future directions may include separate cluster analyses on psychophysical and psychosocial profiles to reveal more subgroups masked by our current cluster approach.

A higher proportion of patients in the high somatic symptoms cluster reported their back pain radiating down their leg and reported their back pain to display neuropathic-like characteristics. Neuropathic pain, usually viewed only as to be a result of lesions affecting the somatosensory system, has also been shown to be triggered in parallel by psychological factors. In 2015, Dimova et al. demonstrated that healthy adults who displayed a pessimistic life attitude also displayed neuropathic-like pain patterns after topical capsaicin application (Dimova et al., 2015). Therefore, it is hypothesized that the high proportion of patients reporting a neuropathic-like component for their back pain in the high somatic symptoms cluster may be explained by a high tendency of the patients to focus on their pain-related bodily sensations. However, along with reporting neuropathic-like characteristics, patients in the high somatic symptoms cluster displayed similar thermal and pressure pain thresholds

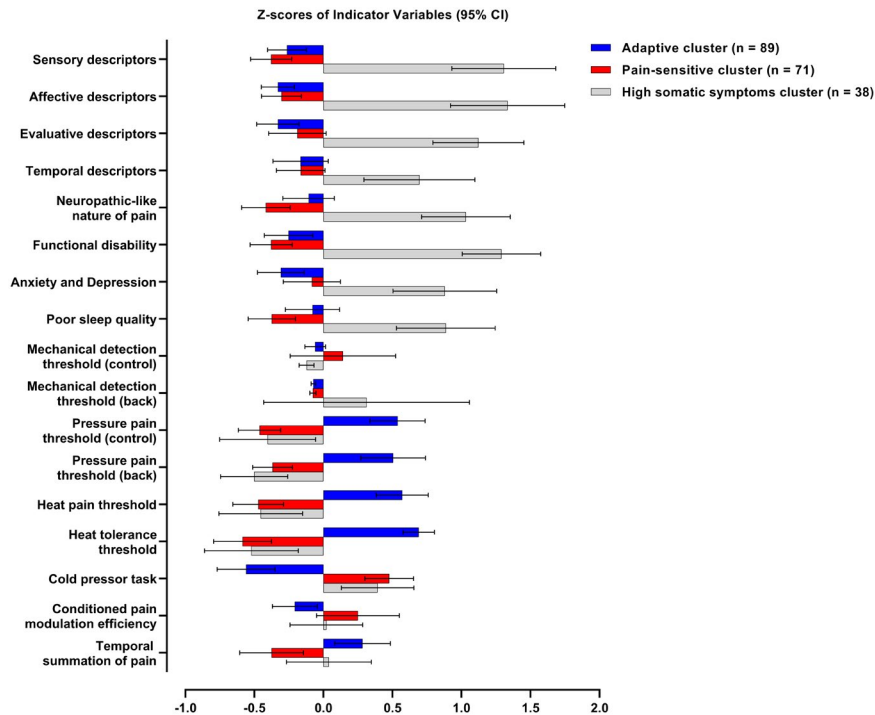


FIGURE 2 Z-scores of the indicator variables. These plots show the mean values and associated 95% confidence intervals of the indicator variables included in the cluster analysis. Each variable displayed in the figure was normalized to have a mean of 0 and SD 1. Z-scores >0 represent values higher than the mean of the sample, and z-scores <0 represent values lower than the mean of the sample. DN4, douleur neuropathique 4 questionnaire; FDI, functional disability index; PSQI, Pittsburgh sleep quality index; MDT, mechanical detection threshold; PPT, pressure pain threshold; HPT, heat pain threshold; HTT, heat tolerance threshold; CPT, cold pressor task; CPM, conditioned pain modulation; TSP, temporal summation of pain

to the pain-sensitive cluster, suggesting possible involvement of central and peripheral pain mechanisms. Without the presence of a lesion in the somatosensory system, it may be hypothesized that nociplastic pain may act as the dominant pain mechanism in this cluster of patients such that nociceptive and neuropathic pain are not entirely responsible for the pain (Kosek et al., 2021). Nociplastic pain is defined as “pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain” (Kosek et al., 2016). Recently, clinically useful criteria for nociplastic pain were established such that chronic nociplastic pain was defined as: (1) pain duration >3 months, (2) a regional rather than discrete distribution, (3) not entirely explained by nociceptive or neuropathic pain mechanisms and (4) displaying clinical signs of pain hypersensitivity in the region of pain. The presence of a history of pain hypersensitivity in the region of pain and defined co-morbidities (e.g. sleep disturbance and cognitive problems) strengthen the probability of nociplastic pain (Kosek et al., 2021). Some patients in the high somatic symptoms cluster meet the requirements of chronic nociplastic pain such that they may report regional pain distribution (i.e. variable pain intensity across

the back), report pain that cannot entirely be explained by nociceptive or neuropathic mechanisms, show clinical signs of pain hypersensitivity (i.e. low thermal and pressure thresholds) and psychosocial co-morbidities (Nijs et al., 2021).

4.2 | Clinical implications

The management and treatment of chronic back pain may remain a challenge. Current back pain guidelines highlight multidisciplinary management using a biopsychosocial model as the standard of care. A comprehensive use of exercises, physical therapy, cognitive behavioural therapy, and medical treatments with a active commitment of the patients and parents are associated with positive clinical outcomes (Randall et al., 2018; Simons et al., 2018). Studies investigating quantitative sensory testing and psychosocial factors in relation to musculoskeletal pain have shown the importance of a multidimensional assessment (Georgopoulos et al., 2019; Holbeck et al., 2016; Hwang et al., 2017; Teles et al., 2019; Tham et al., 2016). Georgopoulos et al. (2019) highlight that the baseline assessment with quantitative sensory testing was a valuable instrument to predict clinical outcomes

TABLE 4 Differences between clusters regarding psychosocial and psychophysical characteristics

Variable	Adaptive cluster (n = 89)	Pain-sensitive cluster (n = 71)	High somatic symptoms cluster (n = 38)	χ^2 value	p-value
Descriptores of pain used, Mean (%) \pm SD					
Sensory	14.98 \pm 7.77 ^c	13.64 \pm 7.18 ^c	33.21 \pm 13.3 ^{a,b}	63.13 [†]	<0.001
Affective	4.96 \pm 6.79 ^c	5.27 \pm 7.27 ^c	24.92 \pm 15.11 ^{a,b}	59.01 [†]	<0.001
Evaluative	27.06 \pm 15.49 ^c	30.09 \pm 18.70 ^c	58.16 \pm 21.47 ^{a,b}	49.83 [†]	<0.001
Temporal	21.66 \pm 13.14 ^c	21.68 \pm 10.27 ^c	33.53 \pm 16.87 ^{a,b}	19.18 [†]	<0.001
Neuropathic component, n (%)					
Mean score of DN4 questionnaire, Mean \pm SD	2.24 \pm 1.84 ^{b,c}	1.59 \pm 1.55 ^{a,c}	4.61 \pm 2.03 ^{a,b}	50.82 [†]	<0.001
Likely neuropathic	18 (20.2)	10 (14.1)	27 (71.1)	44.64*	<0.001
Not likely neuropathic	71 (79.8)	61 (85.9)	11 (28.9)		
Functional Disability, n (%)					
Mean score of FDI, Mean \pm SD	12.82 \pm 8.58 ^c	11.52 \pm 6.61 ^c	28.72 \pm 8.91 ^{a,b}	63.06 [†]	<0.001
None or minimal	48 (53.9)	40 (56.3)	1 (2.6)	94.12*	<0.001
Mild	23 (25.8)	21 (29.6)	6 (15.8)		
Moderate	16 (18.0)	9 (12.7)	12 (31.6)		
Severe	2 (2.2)	0	19 (50.0)		
Anxiety and Depression Symptoms, n (%)					
Mean T-score of RCADS, Mean \pm SD	41.52 \pm 9.95 ^c	44.30 \pm 10.84 ^c	56.24 \pm 14.17 ^{a,b}	28.36 [†]	<0.001
Below clinical threshold	88 (98.9)	68 (95.8)	27 (71.1)	32.21*	<0.001
Borderline	1 (1.1)	1(1.4)	3 (7.9)		
Above clinical threshold	0	2 (2.8)	8 (21.1)		
Sleep Quality, n (%)					
Mean global score of PSQI, Mean \pm SD	6.70 \pm 3.25 ^c	5.68 \pm 2.51 ^c	10.07 \pm 3.79 ^{a,b}	32.50 [†]	<0.001
Good sleep quality	26 (29.2)	25 (35.2)	3 (7.9)	9.83*	0.007
Poor sleep quality	63 (70.8)	46 (64.8)	35 (92.1)		
MDT (g), Mean \pm SD					
Control area	0.42 \pm 0.58	0.75 \pm 2.66	0.31 \pm 0.27	0.45 [†]	0.800
Affected area	0.56 \pm 0.95	0.53 \pm 1.14	5.34 \pm 28.04	1.38 [†]	0.501
PPT (N), Mean \pm SD					
Control area	35.58 \pm 14.05 ^{b,c}	20.75 \pm 9.53 ^a	21.62 \pm 15.68 ^a	53.12 [†]	<0.001
Affected area	35.18 \pm 19.41 ^{b,c}	19.94 \pm 10.49 ^a	17.62 \pm 12.92 ^a	43.36 [†]	<0.001
HPT (°C), Mean \pm SD					
Control area	41.04 \pm 2.83 ^{b,c}	37.74 \pm 2.47 ^a	37.80 \pm 2.92 ^a	51.18 [†]	<0.001
Affected area	46.82 \pm 1.30 ^{b,c}	43.75 \pm 2.13 ^a	43.9 \pm 2.48 ^a	94.47 [†]	<0.001
CPT average pain score NRS (0–10), Mean \pm SD					
Control area	5.68 \pm 2.28 ^{b,c}	8.08 \pm 1.73 ^a	7.89 \pm 1.85 ^a	52.13 [†]	<0.001
Affected area					
CPM, n (%)					
CPM efficiency (%), Mean \pm SD	–38.37 \pm 33.00	–18.73 \pm 54.40	–28.53 \pm 34.40	3.80 [†]	0.149
Inefficient	17 (19.1)	23 (32.4)	11 (28.9)	4.14*	0.387
Suboptimal	21 (23.6)	16 (22.5)	8 (21.1)		
Optimal	51 (57.3)	32 (45.1)	19 (50.0)		
TSP, n (%)					
TSP pain score NRS (0–10), Mean \pm SD	0.68 \pm 1.99 ^b	–0.69 \pm 2.02 ^a	0.17 \pm 1.94	15.31 [†]	<0.001
No presence	70 (78.7)	66 (93.0)	35 (92.1)	10.43*	0.005

TABLE 3 (Continued)

Variable	Adaptive cluster (n = 89)	Pain-sensitive cluster (n = 71)	High somatic symptoms cluster (n = 38)	χ^2 value	p-value
Presence	19 (21.3)	5 (7.0)	3 (7.9)		

Note: p-values ≤ 0.05 are bolded.

Abbreviations: CPM, conditioned pain modulation; CPT, cold pressor task; DN4, douleur neuropathique 4 questionnaire; FDI, functional disability index; HPT, heat pain threshold; HTT, heat tolerance threshold; MDT, mechanical detection threshold; PPT, pressure pain threshold; PSQI, Pittsburgh sleep quality index; RCADS, revised children's anxiety and depression scale; SD, standard deviation; TSP, temporal summation of pain.

^aSignificant difference with cluster 1

^bSignificant difference with cluster 2.

^cSignificant difference with cluster 3.

*Chi-squared test statistic.

†Kruskal-Wallis 1-way analysis of variance chi-squared test statistic.

including disability in patients with musculoskeletal pain. Improving the diagnostic process by identifying 'clusters' of patients with chronic back pain based on results of quantitative sensory testing, pain-related outcomes and psychosocial factors may help clinicians provide an improved individualized care to patients (Vega et al., 2018).

Exercises, physical therapy and psychological therapies are aimed to focus on helping patients return to their desired level of functioning through progressive engagement in previously avoided activities and a self-management approach to pain (Simons et al., 2018; Vega et al., 2018). Studies targeting the central pain processes have used physical activity to reduce the presence of temporal summation pain (Bishop et al., 2011; Pack et al., 2018). Therefore, the patients belonging to an adaptive cluster who display temporal summation of pain, possibly arising from central facilitation, may benefit from a multidimensional programme centred on physical activity (Mirek et al., 2019).

Psychological therapies, delivered individually or in groups in the paediatric chronic pain population, have been shown to reduce pain symptoms, disability and negative affect, but also modify social environmental factors to enhance functional status (Fisher et al., 2018). Hence, a multicomponent approach focused on psychological therapeutic interventions addressing anxiety, depression and poor sleep quality and on the probable pain hypersensitivity may be more beneficial for patients that are grouped in the high somatic symptoms cluster who display more functional disability, mental distress and sleeps problems.

Pharmacological treatments and interventional procedures are mainly supported through studies conducted in adults. Clinical trials in adults suggested that sodium channel modulators such as local anaesthetics could be useful to treat pain conditions associated with peripheral sensitization (Demant et al., 2014; Mainka et al., 2016). Moreover, patients with potential involvement of central pain processes could benefit more from gabapentinoids, inhibiting central neuronal sensitization (Granovsky &

Yarnitsky, 2013). Therefore, patients belonging to the pain-sensitive cluster with possible involvement of central and peripheral pain mechanisms may benefit from a multidimensional program centred on pharmacological or interventional strategies.

4.3 | Limitations and conclusion

There are certain limitations to this study that should be explicit. First, healthy controls were not tested so it is unknown if all pain-free children would fall into one cluster, a new cluster or have a variety of pain profiles as highlighted by Bair et al. (2016). Furthermore, the exclusion of healthy controls limits the extent of the involvement of the underlying nociceptive mechanisms in chronic musculoskeletal pain being clinically relevant. However, the objective of the study was to identify and describe profiles of patients to identify potential treatment responders and ultimately lead to personalized treatment. The second limitation was the cross-sectional nature of the study such that the long-term stability over weeks or months was not studied in this cohort. Therefore, it is unknown whether patients shift from one cluster to another depending on if a therapeutic intervention was given. Future work, conducting a prospective study that includes healthy controls to determine which psychophysical profile is a risk factor to chronic back pain and/or to determine whether a tailored treatment approach based on the clinical profile of the patient is beneficial, is warranted.

In conclusion, despite different pathologies, this study identified clusters of children and adolescents experiencing chronic back pain based on physical and psychosocial profiles. The assessment of chronic back pain should be comprehensive to assess multiple elements contributing to pain, including pathophysiology, somatosensory functioning, and psychosocial factors to improve multidisciplinary pain management.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

All authors contributed to data analysis, drafting or revising the article, gave final approval of the version to be published and agree to be accountable for all aspects of the work.

DATA AVAILABILITY STATEMENT

The data and code used to support the findings of this study are available from the corresponding author upon request.

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