CLINICAL SCIENCE

Sleep, stress, neurocognitive profile and health-related quality of life in adolescents with idiopathic musculoskeletal pain

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OBJECTIVES: The aims of this study were to measure levels of sleep, stress, and depression, as well as health-related quality of life, and to assess the neurocognitive profiles in a sample of adolescents with idiopathic musculoskeletal pain.

METHODS: Nineteen adolescents with idiopathic musculoskeletal pain and 20 age-matched healthy control subjects were evaluated regarding their levels of sleep and stress, as well as quality of life, and underwent neurocognitive testing.

RESULTS: The sample groups consisted predominantly of females (84%), and the socioeconomic status did not differ between the two groups. In addition, the occurrence of depressive symptoms was similar between the two groups; specifically, 26% of the idiopathic musculoskeletal pain patients and 30% of the control subjects had scores indicative of depression. Teenagers in the group with idiopathic musculoskeletal pain reported poorer quality of life and sleep scores than those in the control group. Regarding stress, patients had worse scores than the control group; whereas 79% of the adolescents with idiopathic musculoskeletal pain met the criteria for a diagnosis of stress, only 35% of the adolescents in the control group met the criteria. In both groups, we observed scores that classified adolescents as being in the resistance phase (intermediate) and exhaustion phase (pathological) of distress. However, the idiopathic musculoskeletal pain group more frequently reported symptomatic complaints of physical and emotional distress. The neurocognitive assessment showed no significant impairments in either group.

CONCLUSION: Adolescents with idiopathic musculoskeletal pain did not exhibit cognitive impairments. However, adolescents with idiopathic musculoskeletal pain did experience intermediate to advanced psychological distress and lower health-related quality of life, which may increase their risk of cognitive dysfunction in the future.

KEYWORDS: Fibromyalgia; Adolescent; Psychological Distress; Sleep.

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INTRODUCTION

Musculoskeletal pain is a common complaint in children and adolescents, presenting in 1 to 15% of the apparently healthy population (1–3). Idiopathic musculoskeletal pain (IMP) is defined as the presence of intermittent pain in three or more body regions for a period exceeding three months (4) that cannot be explained by any other particular disease. IMP appears predominantly in females between 5 and 15 years of age (5).

Recent studies have shown that IMP pain symptoms are the result of several factors and that the etiology of musculoskeletal pain must therefore have multiple causes, which may be correlated. Intrinsic factors include a low threshold for pain, female gender, the presence of hypermobility and stress. Extrinsic factors include previous painful experiences, social deprivation, physical and sexual abuse, parental behavior models, pain, sleep disturbances and low physical fitness (6–10). Moreover, cognitive deficits and emotional distress may decrease the ability to cope with pain and other stress factors associated with chronic disease (11,12).

Sleep disorders may lower the threshold for pain (13), and the interaction between sleep and pain probably varies according to

No potential conflict of interest was reported.

individual differences in psychological and behavioral sensitivity. One possibility presented in the literature for the origin of these symptoms is the involvement of the hypothalamic-pituitary-adrenal (HPA) axis, suggesting that the origin of the symptoms of fibromyalgia and IMP is related to stress responses (13).

A wider understanding that adolescents and young adults are susceptible to external stimuli and psychosocial distress is essential for the development of effective IMP management. In addition, because stress manifests both psychologically and physically, the differential diagnosis between physical and mental morbidity is not always easy.

Changes in cognitive functioning and mood abnormalities may also be observed in patients with IMP. Neuropsychological studies have shown impairments in functions such as memory and attention in adults with fibromyalgia (one of the primary types of IMP) (14–17). However, we did not find neurocognitive studies that focused on children and adolescents with musculoskeletal pain in the current literature.

In our clinical practice, we have observed the adverse outcomes of IMP in children and adolescents, which include frequent absence from school, difficulty in social relationships, and greater demand for family care, leading to financial stress and work absences due to medical appointments.

In response to the lack of studies on cognitive functioning, sleep, stress, neurocognitive profiles and health-related quality of life (HRQL) in children and adolescents with IMP, our objectives in this study were the following: 1) to assess the neurocognitive functioning of IMP patients to determine whether there is an early occurrence of cognitive deficits (which have been thoroughly documented in adults) and 2) to investigate factors such as sleep, stress, depression, family history of pain, behavior and HRQL in a clinical sample of IMP patients.

METHODS

Study design: This study had a cross-sectional design.

Patients: Our Pediatric Musculoskeletal Pain Outpatient Clinic opened in May 2008 as part of the Pediatric Rheumatology Unit, Department of Pediatrics. It is coordinated by three pediatric rheumatologists and consists of a team of pediatricians, psychologists, nutritionists, physical therapists, a social worker, and a dentist. All cases were evaluated and discussed by the entire team. Since 2008, 120 patients with IMP between 4 and 18 years of age have been assessed. In the present study, we included consecutive patients with an IMP diagnosis.

Study group: Thirty-nine adolescents, aged 13–16 years, of both genders were divided into two groups: a) 19 patients with IMP randomly selected according to their availability to participate in the study and b) 20 control adolescents matched for gender, age, level of education, and socioeconomic level. The age group for this study was determined according to standardizations required by the tests used in the assessment protocol.

Exclusion criteria for both groups included the presence of neurological comorbidity (e.g., epilepsy, tumors, head trauma); psychiatric disorder (e.g., personality disorders, severe depression, and diagnosed anxiety disorders); malnutrition (measured by means of clinical examination); and low non-verbal reasoning (up to a score of 25, as measured by Raven's Colored Progressive Matrices (18)). In addition, participants who had taken any psychotropic medication for at least six months prior to the study were excluded.

Controls: The control group comprised healthy adolescents, without chronic diseases or rheumatic complaints, attending routine clinical follow-up visits at the Department of Pediatrics Adolescence Outpatient Clinic.

Procedures

The study was approved by the local ethics committee (protocol 0461/08). Adolescents and their parents signed a consent form. Subjects were evaluated individually by the same psychologist (J.M.), who was trained and experienced in the use of evaluative techniques. Evaluations took place in a soundproof, closed room where the subjects' responses would not be affected by external stimuli.

Evaluations: The interview was adapted from a survey designed by Santos (2002) (19) and investigated clinical, neuromotor, and psychosocial development. The questionnaire included items related to pregnancy, birth and development, schooling achievements and possible learning and/or health problems.

The behavioral assessment consisted of the following scales and inventories:

1. Survey on socioeconomic class [Scale for Assessment of Socioeconomic Status by the Brazilian Association of Research Companies ABEP/2008 (ANEP, Associação Nacional de Empresas de Pesquisa) (20); participants were classified into five categories: Class A (35–46 points), Class B (23–34 points), Class C (14–21 points), Class D (8–13 points), and Class E (0 to points 7 points).
2. Depression (Beck Depression Inventory, BDI) (21); scores>9 were indicative of a depressive status.
3. HRQL – Global Scale for Quality of Life (EGQV) (22).
4. Quality of sleep (Sleep Disturbance Scale for Children, SDSC) (23).
5. Screening for behavioral and attention abnormalities [Assessment for Attention Deficit Hyperactivity Disorder (EDAH, Escala para la evaluación del transtorno por déficit de atención com hiperatividad] (24); scores>12 were suggestive of behavioral and attention abnormalities.
6. Psychological distress (Lipp's Stress Symptoms Inventory for Adults, LSSI) (25); LSSI identifies and classifies physical and psychological symptoms according to the three stages of stress: alarm (initial stage - >6 points in domain A), resistance (intermediary stage - >3 points in domain B), and exhaustion (stage when diseases may occur in more susceptible organs - >8 points in domain C).

A neuropsychological assessment was performed using the following tests:

1. Raven's Progressive Matrices Test: measures general intelligence (18).
2. Brazilian Children's Test of Pseudoword Repetition (26): assesses the 'phonological loop' component of working memory.
3. Semantic and Phonologic Verbal Fluency Test (27): measures semantic memory and executive function. For the semantic fluency assessment, the 'Animals' category was utilized, and to assess phonologic fluency, the letters F, A, and S were utilized.

4. Digit span (28): forward order assesses short-term memory, and reverse order assesses working memory.
5. Corsi Block-Tapping Test (29): forward order assesses visual-spatial short-term memory, and reverse order assesses the central executive component of working memory.
6. BEM-144 Visual Memory: A) Visual Recognition of Abstract Patterns (VRAP) and B) Complex Figure Copy and Reproduction (FCS) (30); measures episodic memory.
7. Free words recall (31): assesses episodic memory and consists of two word lists of 15 words each (List 1: words with no semantic association and List 2: triad of words semantically related by positions 7, 8, and 9 on the list and having no semantic association in other positions); also assesses semantic categorization in information recall, i.e., a higher number of words are recalled due to semantic similarity between some of them.
8. WMS Story Recall (32): measures long-term memory of short stories with information semantically arranged.

For the VRAP (item 6A), Free words recall (item 7), and WMS Story Recall (item 8) tasks, participants were requested to perform an immediate recall and a delayed recall after a 20-minute interval. In the FCS test (item 6B), before immediate and delayed recall, participants were also asked to do a copy of the drawing as a measurement of visual-constructive functions.

Statistical analyses

Collected data were analyzed with STATISTICA software (StatSoft Incorporation 1984–2004, Version 7.0).

The results of the descriptive data analyses were obtained in terms of the means, standard deviations, and percentages. For inferential analyses, the Student t-test was carried out to compare scores between the pain group and the control group in the neuropsychological tests and behavioral scales. An additional analysis was performed, using Tukey HSD Test and unequal HSD Test, in order to complete the analysis of the obtained results. Contrasts in the results of the participants inside the group, when observed, were analyzed with Tukey HSD Test and an unequal HSD Test. A significance level of 5% was used.

RESULTS

There was a predominance of females among the study population (16/19 in the IMP group [84%] and 17/20 in the control group [85%]). The demographics of the study population are presented in Table 1. The socioeconomic classification of the sample was similar between the two groups ($p = 0.48$), with most subjects were classified in the B2 class.

There were no differences between the two groups with respect to symptoms of hyperactivity and attention deficit (EDAH). The EDAH scores were below the cutoff point for hyperactivity and attention deficit. With regard to the BDI scale, five patients (26%) in the IMP group presented scores indicative of depression (score >9), whereas five participants (25%) presented the same indicative of depression in the control group. These subjects were referred for a clinical psychological consultation. It should be noted that the scales were not used to confirm the diagnosis of depression and anxiety but were only used as screening tools.

Concerning the HRQL as assessed from the EGQV, significantly lower scores were found in the IMP group compared with the control group ($p = 0.0318$). In addition, significantly lower sleep scores, as measured by the SDSC scale, were noted in the IMP group ($p = 0.0361$) (Table 2).

Regarding distress, LSSI scale analysis was performed according to distress stages (alarm, resistance, and exhaustion), and differences were observed between the IMP and control groups. The total LSSI scale score showed that 79% of the adolescents in the IMP group met the criteria for a stress diagnosis, whereas only 35% of the control adolescents met these criteria. Both groups showed a predominance of distress in the resistance stage. In addition, adolescents with IMP had significantly higher scores in the resistance stage ($p = 0.009$) and the exhaustion stage ($p = 0.023$) (Table 3). Furthermore, IMP patients presented more symptomatic complaints of stress than the control group in both the physical ($p = 0.013$) and emotional ($p = 0.030$) aspects of stress.

We observed differences in performance between the two groups in immediate recall during the neuropsychological assessment free recall test (list 2). Specifically, the control group performed better than the IMP group ($p = 0.05$).

The results obtained from all neuropsychological tests are presented in Table 2. Additional exploratory analyses of variance or t-tests were conducted by subdividing the sample into two subgroups (group 1 = 13- and 14-year-olds, N = 12; group 2 = 15- and 16-year-olds, N = 27) as independent variables to investigate age-related differences in neurocognitive tasks. However, there were no significant differences between the two age groups.

Table 1 - Demographics of and behavioral scale scores [mean ± (SD)] in the sample population.

	IMP Group (N = 19)		Control Group (N = 20)			
	Mean (SD)	Min-Max	Mean (SD)	Min-Max	t-value	*p*-value
Age (y)	14.7 (0.99)	13–16	14.7 (0.97)	13–16	−0.42	0.96
Schooling (y)	8.5 (1.26)	6–11	8.6 (1.23)	6–11	−0.05	0.95
ABEP	23.7 (4.85)	15–33	25.5 (4.78)	15–33	−1.14	0.26
SDSC	29.3 (12.57)	8–56	20.5 (13.02)	6–42	2.17	0.03*
EGQV	17.2 (3.99)	4–22	19.4 (1.76)	16–23	−2.23	0.03*
BDI	7.6 (6.16)	0–21	5.31(5.15)	0–15	1.31	0.19
Pain onset age	8.95(3.46)	3–13	-	-	-	

IMP Group = group of adolescents with musculoskeletal pain; SD = standard deviation; Min-Max = minimum and maximum values of the obtained scores; ABEP = Scale for Socioeconomic Class Status; SDSC = Sleep disorder scale for children; EGQV = Global Scale for Quality of Life; BDI = Beck's Depression Inventory; (*) significant results based on the Student's t-test.

Table 2 - Neuropsychological assessment in adolescents with IMP (N = 19) and controls (N = 20) (mean ± [SD]).

Test scores	IMP Group		Control Group			
	Mean (SD)	Min-Max	Mean (SD)	Min-Max	t-value	*p*-value
Raven's Progressive Matrices Percentile	47.10 (3.36)	42–55	46.50 (1.82)	43–49	0.70	0.17
BCPR	37.42 (1.95)	33–40	38.20 (0.77)	37–40	–1.65	0.12
V.F. Letter F	9.90 (3.71)	3–16	9.65 (2.58)	5–15	0.24	0.81
V.F. Letter A	9.05 (3.06)	4–17	8.45 (2.30)	4–14	0.69	0.49
V.F. Letter S	8.05 (2.90)	3–14	9.20 (2.40)	6–14	−1.35	0.18
V.F. Animals	16.21 (2.92)	10–22	17.20 (2.57)	13–24	−1.12	0.27
Forward Digit span	7.89 (2.16)	5–13	8.30 (1.21)	6–10	−0.72	0.48
Backward Digit span	5.26 (1.79)	3–9	6.05 (1.54)	6–10	−1.47	0.15
FO Corsi's span	5.47 (1.26)	3–8	5.5 (0.76)	4–7	−0.07	0.94
BO Corsi's span	5.21 (1.03)	4–7	5.65 (0.93)	4–7	−1.39	0.17
I VRAP	18.53 (3.75)	11–24	19.25 (3.96)	11–23	−0.59	0.56
D VRAP	18.05 (4.17)	10–24	19.50 (3.31)	11–23	−1.20	0.24
FCS C	9.37 (1.31)	6.5–12	9.37 (1.57)	7–12	−0.14	0.99
FCS IR	6.10 (2.38)	2.5–10	6.72 (2.04)	3–11.5	−0.87	0.39
FCS LR	5.79 (2.17)	3–9.5	5.87 (1.91)	2.5–10	−0.13	0.90
I Word List 1	5.63 (1.67)	3–9	6 (1.62)	4–10	−0.70	0.49
D Word List 1	3.31 (1.67)	1–7	2.75 (1.62)	0–6	1.07	0.29
I Word List 2	5.05 (2.30)	1–9	6.4 (1.96)	3–10	−1.97	0.05*
D Word List 2	2.68 (1.97)	0–6	3.35 (1.46)	1–6	−1.20	0.24
I WMS Story 1	14.68 (4.41)	7–25	15 (3.23)	9–21	−0.25	0.80
D WMS Story 1	12.89 (3.23)	6–19	13 (3.42)	7–18	−0.09	0.92
I WMS Story 2	13.16 (3.93)	7–20	11 (3.85)	4–18	1.73	0.09
D WMS Story 2	12.10 (3.16)	7–17	10.15 (4.34)	2–18	1.60	0.12

BCPR = Brazilian Children's Test of Pseudoword Repetition; V.F. = Verbal fluency; FO = forward order; BO = backward order; I = immediate recall; D = delayed recall; FCS C = FCS Task - Copy; FCS IR = FCS Task – Immediate Reproduction; FCS LR = FCS Task – Late Reproduction. (*) significant result based on the Student's t-test.

DISCUSSION

Some physicians who follow children and adolescents with recurrent pain consider the physical but not the psychological aspects of pain. This perspective may lead to incomplete and ineffective treatment approaches, resulting in symptom persistence and a subsequent significant decrease in HRQL. The main objective of this study was to assess the neurocognitive profile of patients with IMP compared with a control group, with a focus on possible memory impairments. Furthermore, the occurrence of stress, depression, behavioral disturbances and quality of life were assessed.

Our finding of a predominance of IMP in females (84%) corroborates previous reports in the literature (5). Gedalia et al. (33) evaluated 59 children and adolescents with musculoskeletal pain and found that 80% were female. The prevalence of IMP among females is hypothesized to be a result of the following factors: genetic, hormonal, and environmental (34). In addition, factors related to hypersensitivity may also be involved (35). Garcia et al. (35) investigated differences in the pain threshold for healthy individuals, and they found a lower pain threshold for pain trigger points in women compared with age-matched men.

Research on the etiopathogenesis of fibromyalgia has shown psychological factors to be core IMP elements in adults and children (36–38). For the clinical diagnosis of mood (affective) disorders, a detailed psychiatric history is very important; however, the BDI scale is a reliable tool that aids in depression screening and in the recognition of subclinical markers that do not achieve the required criteria for a formal diagnosis (but suggests the possibility of future psychiatric disorders). In our sample, no difference was found between the groups with regard to the occurrence of depressive symptoms, as described in other studies involving adult subjects (39,40). In addition, our data are consistent with those of studies performed in adolescents with IMP (36). In another study, the detection (39) of depressive symptoms was based on an analysis of patient surveys, which did not include a control group. The results indicated that adolescents who fulfilled the criteria for a diagnosis of fibromyalgia presented higher susceptibility to emotional difficulties and were at risk of developing psychiatric comorbidities similar to those seen in adults (75 to 81%) (41).

Complaints regarding stress and sleep changes are directly related to chronic and recurrent pain in both animal and human models (42,43). In addition, studies have demonstrated the impact of stress and poor sleep quality on HRQL (44). According to Graham and Streitel (45), pain may lead to sleep disorders and behavioral disturbances possibly because patients with pain exhibit an increased perception

Table 3 - Lipp's Stress Symptoms Inventory for Adults (LSSI; mean ± [SD]).

	IMP Group (N = 19)		Control Group (N = 20)			
Distress stages	Mean (SD)	Min-Max	Mean (SD)	Min-Max	t-value	*p*-value
Alarm	3.63 (2.71)	0–10	2.2 (1.64)	0–5	2.00	0.05
Resistance	5.60 (3.25)	1–12	3.15 (2.18)	0–8	2.75	0.009
Exhaustion	5.47 (3.33)	0–12	3.20 (2.66)	0–10	2.35	0.02

IMP Group = group of adolescents with musculoskeletal pain; SD = standard deviation; Min-Max = minimum and maximum values of the obtained scores.

of psychological stressors in several life aspects (for example, in family, school and social situations) compared with individuals without chronic pain.

Because stress responses were increased among IMP adolescents, it is likely that these individuals may reach a state of exhaustion while coping. In addition, these authors argued that psychological stress, in general, can amplify the association between pain and sleep. Intense pain itself is a powerful stressor, leading to a "snowballing" effect. In our sample, adolescents with chronic pain exhibited higher levels of stress and sleep dysfunction and worse quality of life compared with the control group. The association between depressed mood, stress, pain and sleep dysfunction is likely to be particularly strong in young people who are still developing their abilities to regulate emotion, attention, and behavioral responses to stress (13). Taken together, these findings and those of other studies (13) suggest that multiple stressors may increase the risk of behavioral and health problems, such as the development of anxiety disorders and mood swings.

The results of the neurocognitive assessment indicated that memory deficits were absent, with the exception of the immediate free recall of one 15-item word list. In particular, list 2 assessed the storage of semantic-related words (e.g., milk, cheese, and butter) in intermediary positions (7, 8, and 9). The presence of semantic-related words in intermediary positions leads to a higher item recall due to semantic association (31,46) in healthy subjects. However, although the IMP group of adolescents had been shown to underperform compared with their peers, it is unknown why these adolescents did not take advantage of semantic associations to improve their recall. However, this finding is not very robust because only a single list was used; thus, further investigation is needed (46).

Overall, there were no differences between groups with regard to the measurements of episodic memory in both immediate and delayed recall in either verbal or visuospatial modalities. Therefore, adolescents with IMP exhibited a mnemonic neurocognitive profile similar to that of adolescents without pain. Our findings are different from those of studies using adults (11,12,14–16,45), in which memory deficits were demonstrated.

Some studies showed a more favorable IMP prognosis for adolescents than adults (48,49). However, a follow-up study showed that 80 to 90% of adolescents still report pain after 2 to 3 years (50). Therefore, if individuals with chronic IMP are more affected, it is possible that the present sample failed to show neurocognitive disorders because the subjects were in the early stages of progression in both IMP and emotional distress. However, further studies on adolescents are necessary to develop a deeper understanding of the impact of IMP over time.

Many unanswered questions remain in the area of musculoskeletal pain. One of the most pressing questions refers to how chronic diseases are related to psychiatric symptoms of depression and anxiety: are anxiety and mood disorders the consequences of experiencing symptoms of chronic diseases, or do they fall within the same disease spectrum because they share common risk factors? This study demonstrated the vulnerability of adolescents facing emotional difficulties, taking into account the indicators of stress and depression. Our findings are important because an estimated 75 to 81% of adults meet the criteria for fibromyalgia at least once in their lifetime (51), according to psychiatric diagnoses.

Our findings highlight the need for more comprehensive care for this population, which could be accomplished with interdisciplinary teams consisting of pediatricians, psychologists, nutritionists, and physical therapists. Such collaborative efforts in somatic pain treatment would allow for an integrative view of the individual as a whole. Our observations justify this point of view, as a positive relationship was found between reduced quality of life and stress levels. However, a more thorough exploration of the cognitive, social and emotional consequences of IMP with a larger number of patients is necessary. Furthermore, a comparison of the neurocognitive functioning between adolescents with idiopathic pain and adolescents with organically based pain (e.g., chronic arthropathies) is also needed.

Methodological limitations of the current study included a small sample size and the absence of highly specific measurements of anxiety and mood disorders. However, a more complete investigation of the emotional, social, and cognitive aspects of the lives of adolescents with IMP is ongoing and includes a larger sample size and comparisons of neurocognitive functioning between adolescents with idiopathic pain and adolescents with organically based pain. The current study was initiated before the creation of the PedIMMPACT guidelines established in 2008, which explains the absence of the rating scales for pain and functional capacity that are now considered the gold standard in pain evaluation. The use of these guidelines will also be addressed in our subsequent study.

We believe that traditional and individual interventions are of great importance in the effort to minimize future impairments in the quality of life of IMP patients. Finally, longitudinal studies must be conducted to increase the understanding of how chronic pain leads to memory impairment as a long-term outcome.

Despite the frequency of complaints related to difficulties in memory, there is no evidence of relevant deficits in memory of adolescents with IMP. However, there is evidence that adolescents with IMP experience symptoms of intermediate to advanced phases of stress, alterations in sleep and poorer quality of life compared to adolescents without chronic pain.

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AUTHOR CONTRIBUTIONS

Molina J executed the project and participated in the study design, data collection, data analysis, and article writing. Len C and Santos FH contributed to the study planning, guidance during work development, discussion of the results, and supervision during the article writing. Terreri MT and Hilário MO provided guidance during the data collection and contributed to the discussion of results. Lopes SG and Fraga M participated in the subject recruiting, statistical analysis, and discussion of the results.

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