

Cognitive, emotional, and behavioral profile in children and adolescents with chronic pain associated with rheumatic diseases: A case-control study

*Clinical Child Psychology
and Psychiatry*
1–13

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DOI: 10.1177/1359104518805800
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**Maria Pascali¹, Emilia Matera², Francesco Craig²,
Francesco La Torre³, Paola Giordano¹,
Francesco Margari⁴, Giuseppina Zagaria²,
Mariella Margari² and Lucia Margari⁵**

¹Pediatric Unit, Department of Biomedical Sciences and Human Oncology, Hospital Polyclinic of Bari, University of “Aldo Moro” Bari, Italy

²Unit for Severe Disabilities in Developmental Aging and Young Adults, IRCCS Eugenio Medea, “La Nostra Famiglia”, Brindisi, Italy

³Pediatric Unit, “A. Perrino” Hospital Brindisi, Italy

⁴Psychiatry Unit, Department of Neuroscience and Sense Organs, Hospital Polyclinic of Bari, University of “Aldo Moro” Bari, Italy

⁵Child Neuropsychiatry Unit, Department of Neuroscience and Sense Organs, Hospital Polyclinic of Bari, University of “Aldo Moro” Bari, Italy

Abstract

Background: The prevalence of chronic pain is about 30% in children and adolescents which suffer from severe emotional distress. The aim of this observational study is to investigate cognitive, emotional and behavioral consequences of benign chronic pain in children and adolescents suffering of reumathologic diseases.

Materials and Methods: A total of 49 participants, chronic pain participants (CPPs) and controls (CGPs), affected by rheumatic diseases, were enrolled. Assessment included collection of sociodemographic data, pain characteristics, and administration of Visual Analog Scale (VAS), Depression Inventory for Children and Adolescents (CDI), Conners’ Parent Rating Scales–Revised (CPRS-R), Child Behavior Checklist (CBCL), and Screen for Child Anxiety–Related Disorders (SCARED). For the statistical analysis, Student’s *t*-test for independent samples and Pearson’s correlation were used. The significance value was set at *p* less than .05.

Results: A significant difference of mean scores of CBCL items and of CPRS items between the two groups was found. In CPPs, a significant correlation between VAS and mean scores of several CBCL items and between VAS and mean scores of several CPRS items was found.

Corresponding author:

Lucia Margari, Department of Neuroscience and Sense Organs, Hospital Polyclinic of Bari, University of “Aldo Moro” Bari, Piazza Giulio Cesare I, 70100 Bari, Italy.
Email: lucia.margari@uniba.it

Conclusion: Chronic pain is a real syndrome in which an interdisciplinary treatment should be applied, considering the psychopathological risk, especially in developmental age.

Keywords

Pain, children, behavior, depression, anxiety

Introduction

Pain is “an unpleasant sensory and emotional experience associated with a present or potential tissue damage, or described as such” (Task Force on Taxonomy of the International Association for the Study of Pain, 1994).

Pain is one of the leading reasons for which patients seek medical care (Lorenz, Sherbourne, & Shugarman, 2009; Shi, Langer, Cohen, & Cleeland, 2007), although drug therapy in most cases gives a marginal relief only.

Chronic pain is a continuous or recurrent pain that persists beyond the expected normal time of healing (World Health Organization (WHO), 2012). It is a major epidemiologic issue and an actual social problem in both pediatric and adult patients: some epidemiological studies indicated that the prevalence of chronic pain ranges from 10% to 80% among the general population (Abu-Saad Huijjer, 2010; Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006; Yeo, 2009) and about 30% in children and adolescents (Fuss, Pagè, & Kats, 2011; King et al., 2011). The most common chronic pain in children and adolescents may result from chronic diseases (arthritis, sickle cell disease, and rheumatologic disorders), trauma (physical, thermal, electrical, and chemical injuries), life-threatening diseases (pain in cancer and HIV/AIDS), and idiopathic causes (most headaches and recurrent abdominal pain; WHO, 2012). More specifically, for pediatric branches such as Rheumatology, pain problem is an integral part of the daily sick child, being an integral part of the disease course in about 20% of cases (Benini, 2010). Rheumatologic diseases in children tend in many cases to have a chronic or recurrent course and are characterized by autoimmune inflammatory processes involving joints, organs, and internal systems. They include over 100 different pathologies: juvenile idiopathic arthritis, systemic lupus erythematosus, juvenile dermatomyositis, scleroderma, juvenile spondyloarthropathy, Kawasaki disease, nodular polyarthritis, and many other. Alarm bells are a limping gait, presence of pains in the joints (knees, ankles, elbows, and wrists), lameness, intake of unusual postures with analgesic purposes, rejection of foods that require energetic chewing, unmotivated tiredness, difficulty climbing stairs or grabbing objects, and joint stiffness in the morning, although it is not the only unequivocal symptoms.

Chronic pain is a complex phenomenon—it involves sensory, physiological, and cognitive-behavioral components—in which psychological factors are closely associated with the development and perpetuation of this condition. Children and adolescents with chronic pain are severely impaired in their daily activities, are unable to attend school regularly, lose social relations, alter family interactions, and suffer from severe emotional distress (Abu-Saad Huijjer, 2010; Cucchiari, Schwartz, Hutchason, & Ornelas, 2017; de Almeida, Braga, Lotufo Neto, & Pimenta, 2013; Moore, Derry, Taylor, Straube, & Phillips, 2014; Zernikow et al., 2012).

Although the symptoms of chronic pain, especially in childhood, are not directly involved with morbidity and/or mortality, these patients demand high costs for the health system, so Clinch and Eccleston (2009) have described a “modern public health disaster.”

Research on chronic pediatric pain abounds in the evaluation of etiology, pathophysiological factors, diagnostic processes, pharmacological, and physical treatments (Blackman, Svensson, &

Marchand, 2018; Gmuca et al., 2018; Orava, Provvidenza, Townley, & Kingsnorth, 2018; Pas et al., 2018; Riquelme, do Rosário, Vehmaskoski, Natunen, & Montoya, 2018; Sheehy et al., 2015); on the contrary, although some lines of research exist (Cáceres-Matos, Gil-García, Barrientos-Trigo, Molina, & Porcel-Gálvez, 2018; Vega et al., 2018; Yetwin, Mahrer, John, & Gold, 2018), current data are more lacking in the evaluation of non-physical variables associated with chronic pediatric pain and related potentially complementary interventions.

Considering the above, the purpose of this observational study was to investigate cognitive, emotional, and behavioral components in a group of children and adolescents with chronic pain suffering from rheumatic diseases and in a group of children suffering from the same diseases but without pain. The hypothesis of the study was that children and adolescents with a chronic painful disease presented, unlike children with no chronic painful symptomatology, cognitive, emotional, and behavioral problems that could complicate the course of the disease; in addition, we wanted to evaluate whether the increase in pain intensity could modify the cognitive, emotional, and behavioral variables in study. The evidence of the existence of such additional components could offer suggestions for more targeted and global therapeutic interventions, especially in the developmental age.

Materials and methods

We recruited 49 participants, aged between 8 and 17 years (mean=11.45, standard deviation (SD) = ± 2.45). All the enrolled participants respected the following inclusion criteria: age up to 18 years, both sexes, and diagnosis of a rheumatic disease.

Participants were divided into two groups: the first group ($N=29$) included participants with a rheumatic disease and pain symptoms lasting for at least 3 months (CPPs), with a pain cutoff corresponding to a 2 cm score (“mild pain”) on the Visual Analog Scale (VAS). The second group ($N=20$) included participants with a rheumatic disease and with a pain cutoff less than 2 cm on the VAS scale for at least 6 months, therefore free enough from the memory of the previous painful condition, which was considered the control group (CGPs). Since this is a case–control study, CPPs and CGSP differed only in the presence/absence of pain while they were all bearers of rheumatic diseases. Exclusion criteria included diagnosis of cancer, terminal or other malignant diseases, previous diagnosis of neuropsychiatric disorders, and the inability to comprehend or to give informed consent.

Participants of the CPPs and CGPs groups were enrolled at the Pediatric Unit of the “A. Perrino” Hospital of Brindisi and were subjected to the study procedures from a medical staff formed by neuropsychiatrists of Child and Adolescent Neuropsychiatry Unit, Department of Basic Medical Sciences, Neurosciences and Sense Organs of the University Hospital of Bari. The Ethics Committee of the Azienda Ospedaliero Universitaria Consorziale Policlinico di Bari approved this study (n. 4579, Prot. 1803/C.E of 12/03/2014). In addition, all the study procedure details were explained to the CPPs, the CGPs, and their parents/legal tutors, and a written informed consent was obtained prior to enrollment.

Clinical and sociodemographic features of the sample (age, sex, diagnosis, frequency, duration, and localization of pain) were gathered by the medical staff in data collection files. The following standardized scales were also administered:

- *VAS* (Flynn, van Schaik, & van Wersch, 2004). It is a horizontal line, 100 mm in length, anchored by word descriptors at each end that tries to measure the amount of pain that a patient feels ranging across a continuum from none to an extreme amount of pain. The patient marks on the line the point that they feel represents their perception of their current state, from “no harm, discomfort, pain” to “very bad, aches pain.” The VAS score is determined by measuring in millimeters from the left hand of the line to the point that the patient

marks. The normative values for the intermediate scale scores are not available. This scale is used from 7 years of age.

- *Depression Inventory for Children and Adolescents (CDI) (Kovacs, 1992)*. It is a 27-item scale that rates the severity of symptoms related to depression and/or dysthymic disorder in children and adolescents from 8 to 17 years of age. The CDI is self-rated and symptom-oriented. The 27 items concern sadness, pessimism, anhedonia, misbehavior, self-esteem, guilt, suicidal ideation, crying, irritability, reduction of social interest, indecision, academic difficulties, sleep disorders, fatigue, decrease of appetite, somatic concerns, loneliness, and disobedience. Children and adolescents select the items that best characterize their symptoms during the last 2 weeks. Each response is classified on a 3-point scale (from 0 to 2), and the total score obtained can range from 0 to 54. A total score of 15 is for mild, 20 for moderate, and 25 for severe depression.
- *Conners' Parent Rating Scales-Revised (CPRS-R; Conners, 2007)*. They investigate behavior problems in children and adolescents aged 3–17 years on the basis of information given by parents. The 80 items are divided into different subscales: opposition, social problems, cognitive/inattentive problems, psychosomatic, hyperactivity, anxious-shy, attention deficit hyperactivity disorder (ADHD) index, perfectionism, and Conners' global index. The responses are on a scale of four values: 0=never, rarely; 1=occasionally; 2=often; and 3=very often, frequently. The scores of each scale can then be converted into standardized *T* scores with an average of 50 and a *SD* of 10. As a rule, *T* scores above 60 have interpretative value, while *T* scores from 61 to 70 are considered moderately atypical and *T* scores above 70 are markedly atypical.
- *Child Behavior Checklist for ages 6–18 years (CBCL; Achenbach & Rescorla, 2001)*. It is a diagnostic questionnaire, aimed to identify behavioral problems of children and adolescents, compiled by their parents. The school age version (CBCL 6–18) explores a variety of behavioral and emotional problems such as attention-deficit hyperactivity disorder, oppositional defiant disorder, conduct disorder, childhood depression, separation anxiety, childhood phobia, and a number of other childhood and adolescent issues. Responses are recorded on a Likert-type scale: 0=not true, 1=somewhat or sometimes true, and 2=very true or often true. Similar items are grouped into syndrome scales (aggressive, anxious/depressed behavior, attention problems, rule-breaking behavior, somatic complaints, social problems, thought problems, and withdrawn/depressed) and in several “*DSM-oriented*” scales which take into account the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*). The CBCL also uses a normative sample to create standard scores that compare the raw score with that typical of young people of the same sex and age. The standard score of 50 is considered the average, with a *SD* of 10 points. For each scale, scores below the 93th percentile are in the normal range, scores between the 93rd and 97th percentile are in the borderline range, and scores above the 97th percentile are in the pathological range.
- *Screen for Child Anxiety Related Disorders (SCARED; Birmaher, Khetarpal, Cully, Brent, & McKenzie, 1995)*. It is a self-assessment tool for parents, consisting of 41 elements, used to screen childhood anxiety disorders including general anxiety disorder, separation anxiety disorder, panic disorder, social, and school phobia. The target population is made up of children aged between 8 and 18 years. Severity of symptoms for the past 3 months is rated using a 0- to 2-point rating scale with 0 meaning not true or hardly ever true, 1 meaning sometimes true, and 2 meaning true or often true. A total score ≥ 25 may indicate the presence of an Anxiety Disorder.

Table 1. Clinical and sociodemographic features of CPPs and CGPs.

	CPPs (N=29)	CGPs (N=20)
Age (in years, mean \pm SD)	12.28 \pm 2.92	10.25 \pm 2.31
Gender (N)	Females 20 Males 9	Females 16 Males 4
Diagnosis (N)		
Juvenile idiopathic arthritis	24	17
Acute articular rheumatism	3	
Algodystrophy	1	
SAPHO syndrome	1	
Undifferentiated connective tissue disease		2
Kawasaki disease		1
Pain localization (N)		
Upper limbs (hands, wrists, and elbows)	6	
Lower limbs (hip, knees, ankles, and feet)	7	
Jaw	2	
Eyes	3	
Spine	3	
Polyarthritis	8	
Pain duration (months, mean \pm SD)	8.20 \pm 4.23	

CPPs: chronic pain participants; CGP: control group; SAPHO: Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis; SD: standard deviation.

All the variables were subjected to statistical analysis. Sociodemographic and clinical features of the two groups (CPPs and CGPs) were studied with the calculation of mean values and *SD*. For the analysis of the quantitative variables (total scores of VAS, CDI, and SCARED; items scores of CBCL and CPRS), the Student's *t*-test for independent samples was used. In CPPs, Pearson's correlation for the analysis of the variable "VAS" in respect to each outcome with statistically significant difference between CPPs and CGPs (items scores of CBCL and CPRS) was used. Although CDI, SCARED, CBCL, and CPRS are ordinal variables, we preferred a parametric test because we used the numeric scores obtained in each test. Considering the different structure of the tests used and the purposes of our study, we sometimes referred to the total scores (VAS, SCARED, and CDI) and sometimes the item scores (CBCL and CPRS). Putting together the results obtained, the independent variables that showed a significance value in univariate analyses were included as predictors or associated factors in the multiple linear regression analysis. The R^2 value was calculated in order to evaluate the goodness of fit about the model and included risk factors (observed versus estimated). The significance value was set at *p* less than .05. For statistical processing, we used the data processing program statistical package for social science, version 20.0 (IBM Corporation, New Orchard Road, Armonk, NY, USA).

Results

Clinical and sociodemographic features of CPPs and CGPs are reported in Table 1.

In both groups, females prevailed over males (69% in CPPs and 80% in CGPs), and the most frequent diagnosis was juvenile idiopathic arthritis (83% in CPPs and 85% in CGPs). In CPPs, pain was more frequently localized to upper limbs (21%), lower limbs (24%), or both (28%). The mean duration of pain was 8.20 \pm 4.23 months.

Table 2. Pearson's correlation between items of CBCL and VAS scores.

CBCL		VAS
Anxious/depressed	Pearson's correlation	.295
	Sig. (two-tailed)	.042*
	<i>N</i>	49
Withdrawn/depressed	Pearson's correlation	.318
	Sig. (two-tailed)	.028*
	<i>N</i>	49
Somatic complaints	Pearson's correlation	.311
	Sig. (two-tailed)	.032*
	<i>N</i>	49
Attention problems	Pearson's correlation	.347
	Sig. (two-tailed)	.016*
	<i>N</i>	49
Aggressive behavior	Pearson's correlation	.358
	Sig. (two-tailed)	.012*
	<i>N</i>	49
Somatic problems	Pearson's correlation	.312
	Sig. (two-tailed)	.031*
	<i>N</i>	49
Rule-breaking	Pearson's correlation	.071
	Sig. (two-tailed)	.634
	<i>N</i>	49
Social problems	Pearson's correlation	.274
	Sig. (two-tailed)	.059
	<i>N</i>	49
Thought problems	Pearson's correlation	.145
	Sig. (two-tailed)	.324
	<i>N</i>	49

CBCL: Child Behavior Checklist; VAS: Visual Analog Scale.

* significant correlation.

CBCL

There was a statistical significant difference of the scores' mean values of the items anxious/depressed ($57.57 + 9.44$ in CPPs and $52.90 + 4.25$ in CGPs; $p = .44$), withdrawn/depressed ($58.14 + 8.86$ in CPPs and $53.35 + 3.73$ in CGPs; $p = .02$), somatic complaints ($60.96 + 7.55$ in CPPs and $56.10 + 6.30$ in CGPs; $p = .02$), attention problems ($54.61 + 4.53$ in CPPs and $51.65 + 1.89$ in CGPs; $p = .00$), aggressive behavior ($53.61 + 4.53$ in CPPs and $51.25 + 2.17$ in CGPs; $p = .03$), and somatic problems ($59.82 + 8.28$ in CPPs and $55.05 + 7.20$ in CGPs; $p = .04$) between CPPs and CGPs. Considering only CPPs, a significant, although small correlation between withdrawn/depressed, somatic complaints, attention problems, aggressive behavior, somatic problems, and VAS scores was found (Table 2). The associated factors were included in a multiple linear regression model with the VAS scores as dependent variable. The corrected $R^2 = .16$ indicated that attention problems ($\beta = -.74$; 95% confidence interval (CI) = $[-.63, -.38]$; $p = .029$) explained 16% of the variance of the VAS score (Table 4).

Table 3. Pearson's correlation between items of CPRS-R and VAS score.

CPRS-R		VAS
Cognitive problems	Pearson's correlation	.353
	Sig. (two-tailed)	.014*
	N	48
Anxiety/shyness	Pearson's correlation	.349
	Sig. (two-tailed)	.015*
	N	48
Social problems	Pearson's correlation	.393
	Sig. (two-tailed)	.006*
	N	48
Physical symptoms	Pearson's correlation	.364
	Sig. (two-tailed)	.011*
	N	48
Oppositional problems	Pearson's correlation	.218
	Sig. (2-tailed)	.136
	N	49

CPRS-R: Conners' Parent Rating Scales–Revised; VAS: Visual Analog Scale.

* significant correlation.

CDI

The mean values of the CDI total scores were higher in CPPs with respect to CGPs, but there were no statistical significant differences of the mean values of CDI total scores between CPPs and CGPs.

SCARED

The mean values of the SCARED total scores were higher in CPPs with respect to CGPs, but there were not statistical significant differences of mean values of SCARED total scores between CPPs and CGPs.

CPRS-R

There was a statistical significant difference of mean values scores of item oppositional (48.69 + 10.19 in CPPs and 43.32 + 6.28 in CGPs; $p=.04$), cognitive problems (50.14 + 11.71 in CPPs and 43.89 + 5.08 in CGPs; $p=.03$), anxiety-shyness (51.52 + 10.85 in CPPs and 44.63 + 6.67 in CGPs; $p=.01$), social problems (52.83 + 13.49 in CPPs and 45.47 + 2.59 in CGPs; $p=.02$), and physical symptoms (56.86 + 14.40 in CPPs and 47.16 + 11.61 in CGPs; $p=.01$) between CPPs and CGPs.

Considering only CPPs, a significant, although small correlation between cognitive problems, anxiety-shyness, social problems, physical symptoms, and VAS scores was found (Table 3). The associated factors were included in a multiple linear regression model with the VAS scores as dependent variable. The corrected $R^2=.16$ indicated that cognitive factors ($\beta=.85$; 95% CI = [.04, .3]) explained 16% of the variance of the VAS score (Table 4).

Table 4. Multiple linear regression analysis between VAS score and subscales of CBCL and CPRS-R.

Model	No standardized coefficients		Standardized coefficients	t	Sig.	Confidence interval 95.0% for B	
	B	SD	Beta			Lower limit	Upper limit
(constant)	16.496	5.589		3.032	.006	5.434	28.457
Anxious/depressed	-.087	.118	-.398	-.739	.47	-.337	.162
Withdrawn/depressed	.053	.125	.229	.427	.675	-.211	.318
Somatic complaints	-.081	.177	-.298	-.461	.651	-.454	.291
Attention problems	-.337	.145	-.740	-2.32	.029*	-.637	-.038
Aggressive behavior	.139	.147	.304	.944	.358	-.171	.449
Somatic problems	-.010	.051	-.071	-.197	.846	-.117	.097
Cognitive problems	.173	.065	.853	2.647	.013*	-.040	.307
Anxiety/shyness	-.004	.062	-.023	-.068	.947	-.135	.127
Social problems	.006	.136	.024	.046	.964	-.280	.293
Physical symptoms	.110	.139	.439	.786	.443	-.185	.404

CPRS-R: Conners' Parent Rating Scales-Revised; CBCL: Child Behavior Checklist; SD: standard deviation.

* significant correlation.

Discussion

Chronic pain is a complex phenomenon that should be considered not only as a symptom but as a real syndrome, in which different factors, not only organic, are involved and influenced such as cognitive, emotional, and behavioral.

In this study, CPPs had significantly higher scores regarding somatic, cognitive (attention), emotional (anxious-depressive symptoms), and behavioral (aggression, oppositional, and relational) problems with respect to CGPs. The absence of pain in CGPs was demonstrated with scores less than 2 cm in the VAS scale.

The presence of more important somatic symptoms in CPPs appeared obvious, but CPPs derived by the comparison between subjects with the same type of pathologies are important to evaluate whether a generic state of disease could be related to cognitive, emotional, and behavioral components.

In this study, CCPs had more cognitive problems such as attentive and concentration difficulties with respect to the control group; these data were confirmed by the results of CBCL and CPRS-R tests and by the reports of several authors which found cognitive/attention problems and, thus, academic difficulties (Kosola et al., 2017; Logan, Simons, & Kaczynski, 2009; Logan, Simons, Stein, & Chastain, 2008; Mifflin, Chorney, & Dick, 2006) in children and adolescents with chronic pain. In contrast, Ho, Bennett, Cox, and Poole (2009) found that despite school absenteeism, children with chronic pain was not lagging behind their peers for both basic cognitive and academic skills, providing some reassurance that they were able to continue to learn.

CPPs had higher scores in the items anxiety/depression of CBCL and anxiety/shyness of CPRS scales with respect to CGPs, with a statistically significant difference. Several previous studies showed that comorbid depression and anxiety were common in chronic pain patients (Cooper et al., 2017; Cucchiario et al., 2017; Cunningham et al., 2016; Gureje, 2007; Khan et al., 2015; Martínez, Gómez-Restrepo, Ramírez, & Rodríguez, 2016; Simons, Sieberg, & Claar, 2012; Vinall, Pavlova, Asmundson, Rasic, & Noel, 2016; Zis et al., 2017). Neurobiological factors (genes,

hormones, and neural networks) shared between chronic pain and symptoms of psychological distress such as anxiety and depression may partly explain their co-occurrence. For example, pain and depression share similar physiological pathways: neuroinflammation and neurological changes in the amygdale and hippocampus were observed in both and antidepressant drugs were effective in treating both (Cucchiario et al., 2017; Gureje, 2007; Ho et al., 2009; Zis et al., 2017). Such results are relevant because youth with co-morbid depression and chronic pain are at an increased risk of thinking about and attempting suicide (Hassett et al., 2013; van Tilburg, Spence, Whitehead, Bangdiwala, & Goldston, 2011). In contrast, in adults, previous studies have found that chronic pain is associated with increased suicide ideation independent of depression (Margari et al., 2013; Miller, Hopkins, & Whorwell, 2004). Anxiety and depression symptoms in turn (Cucchiario et al., 2017; Cunningham et al., 2016; Khan et al., 2015; Martínez et al., 2016; Simons et al., 2017; Vinall et al., 2016), may play a key role in the maintenance of disability, driving them to avoidant behaviors and perpetuating a vicious cycle, which may further decrease youth quality of life (Cunningham et al., 2016; Simons et al., 2012; Tarantino et al., 2013; Vinall et al., 2016).

In addition to internalizing symptoms, in this study, CPPs showed higher levels of aggression with respect to CGPs, with a statistically significant difference, as confirmed by CBCL. In previous studies, the relation between chronic pain and aggression was studied indirectly by considering aggression as a behavioral reaction that derives from angry feelings. The way in which anger is managed has an important effect on disease course and impact; in particular, failure to express one's own anger is related to more intense and frequent pain. However, in chronic pain syndromes, children and adolescents showed a significantly greater tendency to inhibit anger (Cunningham et al., 2016), thus a vicious circle is established in which anger is inhibited by chronic pain and retained anger increases affective component of pain (Thomas, Moss-Morris, & Faquhar, 2006). Results of our study are similar to data obtained from adult sample. Fishbain et al. (2011) studied the prevalence of different types of anger in adults, supporting the clinical perception that many chronic pain patients were angry. Margari et al. (2013) showed that aggression is common in chronic pain patients, supporting the hypothesis that aggression and pain could share a common biological–structural nucleus including several factors (serotonergic/adrenergic/endogenous opioids systems, immunitary system, metabolism), which could clarify the relation between chronic pain and emotional–behavioral components associated with it.

In this study, CPPs had more social and relational problems with respect to CGPs, with a statistically significant difference, as evidenced by the results of CBCL and CPRS-R tests, confirming previous studies in which subjects with chronic pain diseases reported great difficulties in social and family interactions probably because they reach lower levels of education, stopped playing sports, have depressive/anxiety symptoms, and are subjected to hospitalizations (Abu-Saad Huijer, 2010; Cucchiario et al., 2017; de Almeida et al., 2013; Moore et al., 2014).

In addition, this analysis had the objective to evaluate whether the increase in pain intensity could modify the cognitive, emotional, and behavioral variables in study. The increase in the VAS scores was correlated with the increase in the scores of anxious/depressed, withdrawn/depressed, aggressive behavior items of CBCL, and cognitive problems, anxiety/shyness, social problems, and physical symptoms items of the CPRS-R underlining the existence of a consequential relationship between the level of pain perception and the other components mentioned. In literature, only few studies examined these associations. Tarantino et al. (2013) reached different conclusions with respect to our results showing that the way in which children and adolescents with chronic pain express anger had an important effect on the course and the impact of the pain symptoms, because the incapacity to express their own anger was associated with a more frequent and intense pain.

Moreover, the model created with the variables that showed an association with the increase of VAS score in CPPs included attention problems and cognitive problems which explained 16% (corrected $R^2 = .16$) of the variance of the VAS score. Cognitive component seemed to influence the perception of pain, supporting, also in this case, the hypothesis that the co-occurrence of chronic pain and mental health conditions can be explained by the presence of shared neurobiological (genes, hormones, and brain networks) and cognitive factors (attention and memory) that lead to development and/or maintenance of both conditions (Asmundson, Coons, Taylor, & Katz, 2002; Asmundson & Katz, 2009).

Several are the limitations of this study: the small sample size, the inclusion of participants with different diseases (juvenile idiopathic arthritis; acute articular rheumatism; algodystrophy; Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome; undifferentiated connective tissue disease; Kawasaki Disease) and with a different clinical course, pain mechanisms, intensity and seasonal symptoms, which certainly influenced the obtained results, the lack in using specific neuropsychological tests designed to measure intelligence and cognitive ability, and other tests/questionnaires administered directly to children and adolescents.

Although pharmacological and surgical treatments are currently the most common approaches in children and adolescents with chronic pain, future research should be aimed at increasing the knowledge and implementation of multidisciplinary and intensive procedures (Roessler et al., 2016; Zernikow et al., 2012) which include non-pharmacological approaches (support and relationship techniques, behavioral interventions, physical interventions; Cunningham & Kashikar-Zuck, 2013; Hoffart & Wallace, 2014) to introduce more substantial changes in pain management and associated disabilities. There is a need for prospective and interdisciplinary studies to identify the mechanisms that contribute to the development and maintenance of chronic pediatric pain, to perfect interventions that can interrupt these mechanisms, to personalize the treatment of pain, and to control the psychopathological risk of chronic pain, especially in the developmental age.

Authors' Note

Francesco Craig is now affiliated with Unit for Severe Disabilities in Developmental Aging and Young Adults, IRCCS Eugenio Medea, "La Nostra Famiglia", Brindisi, Italy.

Declaration of conflicting interests

The authors declare that they do not have any conflict of interest.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Author biographies

Maria Pascali worked as a practicing physician at the Pediatric Unit of the Polyclinic of Bari. She has a degree in Medicine and Surgery and is currently an internist doctor.

Emilia Matera has a degree in Medicine and Surgery. She has completed a postgraduate degree and a PhD in Child and Adolescent Neuropsychiatry (University of Bari). She currently works at the Child Neuropsychiatry Unit of the Polyclinic of Bari.

Francesco Craig has completed a PhD in Child and Adolescent Neuropsychiatry (University of Bari). He is a clinical psychologist with experience in children and adolescents neurodevelopmental disorders. He is actually a researcher at the Scientific Institute-IRCCS E. Medea.

Francesco La Torre has a degree in Medicine and Surgery and a postgraduate degree in Pediatrics (University of Bari). He currently works at the Pediatrics Unit of the “Perrino” hospital of Brindisi. He is a regional referent (Puglia, Italy) for Pediatric Rheumatology.

Paola Giordano is Director of the Pediatrics Unit of the hospital “Giovanni XXIII” of Bari and of the Postgraduate School in Pediatrics (University of Bari). She is a regional referent (Puglia, Italy) in Pediatric Hematology and Coagulation. Its main areas of interest are pediatric hematology, coagulation and pediatric pain.

Francesco Margari is a Psychiatrist at the U.O. of Psychiatry (Polyclinic of Bari) and an Associate Professor of Psychiatry (University of Bari). At present he carries out assistance and research activity in particular in psychiatric disorders of the adolescent and young adult age.

Giuseppina Zagaria has a degree in Statistical Science. She has worked in the collection and statistical processing of data for various scientific works conducted at the U.O. of Child Neuropsychiatry (University of Bari).

Mariella Margari has a degree in Medicine and Surgery. She is currently a doctor in specialist training at the Child Neuropsychiatry Unit at Polyclinic of Bari.

Lucia Margari is Full Professor in Child Neuropsychiatry and Director of the Postgraduate School in Child Neuropsychiatry (University of Bari). She is also Director of the Child Neuropsychiatry Unit (Polyclinic of Bari). She carries out care, teaching and research activities in neurodevelopmental, psychiatric and neurological disorders of the developmental age.