Empirical classification of children with JIA: a multidimensional approach to pain and well-being

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Abstract

Objective

To investigate the relationship between children's arthritis self-efficacy, trait-anxiety, depression, clinical state of the disease (pain, disability, number of somatic complaints and active joints) and age of the child.

Methods

Trait anxiety and depression of JIA patients were measured by standardized scales (STAIC and CDI). For assessing self-efficacy CASE-scale was used. Pain, CHAQ and active joint count were used as indicators of the disease severity. The K-means cluster procedure was used to classify 145 consecutively recruited patients aged 8 to 15, regarding age, trait-anxiety and depression. One-way multivariate analysis of variance (MANOVA) followed by separate ANOVA's was used for comparisons between the cluster groups. Associations between the cluster groups and the children's self-efficacy were then evaluated using multivariate analysis of variance (MANOVA).

Results

Four cluster groups were identified based on the degree of depression and trait-anxiety. Clinical disease-related parameters differed significantly in the cluster groups. Pain was not necessarily related to the severity of the disease or to the diagnosis (oligoarthritis, oligoextended and polyarthritis). A higher level of self-efficacy was related to lower levels of depression, trait anxiety and pain.

Conclusions

In JIA, the clinical classification of disease activity and severity did not directly correspond with depression and trait-anxiety in children with JIA. Instead, these were regulated by a self-efficacy, which was associated with less pain and somatic complaints.

Key words

Juvenile idiopathic arthritis, self-efficacy, trait-anxiety.

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Introduction

Recently, medical management of juvenile idiopathic arthritis (JIA) has become more aggressive, which has reduced the disease-associated disability (1, 2). However, JIA is still a severe disease, because of its unpredictable course, chronic pain, limitations in daily activities and social participation and it can interfere with lives of the patients. Many children with JIA still have difficulties in adaptation and have a strong sense that their emotional state has been negatively affected by the disease (3), and Sällfors *et al*. (4) indicate that JIA affects common activities in daily life that could make a child dependent on others, thus marginalizing them. Chronic pain often results in an inability to perform day-to-day activities; in children with JIA this can cause disruptions in school attendance and in social activities (5-11). Many children who attempt to participate in school and leisure activities face barriers (*e.g*., lack of understanding by teachers, high steps into buildings) that can limit opportunities for social interaction, and growth of independence from parents (3, 12, 13). Especially challenging are those patients with low measurable disease activity but a high level of pain-connected psychological symptoms, such as anxiety and depression. In clinical work, the pediatric rheumatologist sometimes faces a situation, where the "hard" indicators of disease activity look favorable, but the patient does not feel well. Some of these patients do not respond favorably to the increase in the anti-arthritic therapy. It is both in the patient's and payer's interest to develop tools to find these JIA patients, since they can often be helped by using non-pharmacological therapy and well-focused rehabilitation. Identifying resilience factors that may influence adjustment of these patients is a vital step toward providing appropriate interventions (14, 15).

Self-efficacy is a cognition enhancing the child's sense of control and might thus be a critical resilience factor. Children's arthritis self-efficacy reflects a child's perceived ability to control or manage salient aspects of life with JIA (16, 17). In general, self-efficacy beliefs determine how obstacles are viewed and how they are attributed to: the stronger the self-efficacy, the higher the goals people set themselves, the stronger the coping efforts and the firmer their commitment to overcoming the obstacles (18). Disease-related self-efficacy of children is a crucial factor in functioning with JIA. Its changes relate to changes in the measures of depression, trait-anxiety, health status and disease activity (16-22). Based on a literature review (3, 16-22), we assumed that a number of factors are associated with arthritis self-efficacy beliefs, including disease severity, physical disability and affective state. It was hypothesized that children who report high levels of pain and physical disability, and who are depressed or anxious, would have low self-efficacy.

Because the relationship between disease parameters and pain is not straightforward (23), it is essential to construct a framework which helps to understand the complex and multidimensional aspects of pain in JIA. Trait-anxiety and depression can theoretically be seen as variables regulating the relationship between clinical activity, severity and pain. The primary goal of this study was to explain how these variables are associated with each other, and how self-efficacy is related to them.

We classified the children based on their emotional well-being (trait-anxiety and depression). Age was additionally added as a classifying variable since the age range of the children was wide ranging from childhood to adolescence and coping with a chronic disease differs considerably between these age groups. After clustering we described the clinical parameters (diagnosis, duration of the disease and calculation of active joints), which are characteristics for the subgroups. The associations between the subgroups (based on trait-anxiety and depression) and disease-related parameters (such as pain and somatic complaints and arthritis self-efficacy) were analyzed. The objectives of the study were (1) to investigate whether homogenous subgroups could be identified based on trait-anxiety, depression and age (2) to

compare the differences of the clinical parameters in the subgroups found and to (3) analyze how self-efficacy was related to the cluster subgroups.

Patients and methods

Patients

The inclusion criteria were a JIA diagnosis (24) established at least one year prior to the study and that the child was aged between 8 and 15 years at the start of the study. One hundred and forty-five consecutive patients were recruited over a 6-month period during routine clinical visits. The parent attending with the child was also invited to participate. Only nine parents and/or children refused to participate. Patients were recruited from the Rheumatism Foundation Hospital in Heinola (n=102) with a catchment area covering the whole country, except for the Helsinki Metropolitan Area, which participated by recruiting patients (n=43) from the Paediatric Rheumatology Clinic of the Helsinki University Hospital. All patients and parents signed a study consent form. The mean age of the patients was 11.9 (SD=2.2) years with the diagnosis having been made 6.1 (SD=3.6) years before enrolment. Seventy-three (50.3%) patients had a polyarticular, 25 (17.2%) an extended oligoarticular and 47 (32.4%) an oligoarticular disease. Of the patients, 106 (73%) were girls and 39 (27%) boys.

Methods

Trait-anxiety: Children's trait-anxiety was measured using the STAI (State-Trait Anxiety Inventory for adolescents and adults) (25) and the STAIC (State-Trait Anxiety Inventory for Children aged 9 to 12) (26). The inventory consists of two subscales State-anxiety scale (S-scale) designed to measure subjective, consciously perceived feelings of apprehension, tension and worry, which fluctuate over time and which by design are influenced by the immediate environment and the Trait-anxiety scale (T-scale). The Trait-anxiety scale (T-scale) is an indicator of the level of anxiety experienced by the children and represents how the children generally feel. It is relatively impervious to the conditions under which it is given. Only the T-scales were used in this study. First, the original T-scales were translated. An interdisciplinary team comprising a certified translator, a psychologist, a physiotherapist, a pediatric rheumatologist and a professional, senior researcher translated the original questionnaires from English to Finnish. This translated version was back-translated to English by an independent certified translator, who did not participate in the first translation session. The final agreed version in Finnish was created in a joint session in which all of the above participated, with access to the original, translated and back-translated versions of the T-scales. Since the scales intended for children (STAIC) differs slightly from the adolescents' (STAI), the STAIC and STAI T-scales were combined and adjusted to be scale invariant and thus the minimum value was 0 and the maximum value 30 indicating increasing severity.

Self-efficacy of the children: To measure the self-efficacy of the children, the Self-efficacy Scale for Children with JIA (CASE-scale for children aged 7-17 years) was used (16). It is a questionnaire that measures beliefs in one's efficacy to exercise control over arthritis-related problems. In a previous study we validated the instrument (27) and three factors measuring CASEsom (self-efficacy with somatic symptom) CASEpsych (self-efficacy in psychological functioning) and CASEsoc (self-efficacy in social functioning) were found. Cronbach's alpha for the subscales ranged from 0.77-0.80. The score ranged from 1-5 with higher values indicating stronger self-efficacy.

Depression/mood: To measure depression/mood disturbance of the patients the Child Depression Inventory (CDI) was used (28). The inventory is evaluated for 6 to 17 years old children/adolescents. The Finnish version consists of 26 items to assess a variety of depression symptoms. Scores range from 0 to 2 and in the total score 0 to 52. Higher values indicate increasing severity. The internal consistency of the scale was good (α=0.85).

Functional disability: The Childhood Health Assessment Questionnaire (CHAQ) was used to measure children's functional status (29). The scale assesses performance in eight areas, but in this study the total score was used. Scores range from 0 to 3 with higher scores indicating greater functional impairment**.** The CHAQ has been reported to be reliable and sensitive and it has been validated in a Finnish sample (30).

Pain: A structured pain questionnaire (31, 32), with a 5-level frequency classification of pain (pain seldom or never, once a month, once a week, more than once a week, almost daily) was used. The questionnaire has been validated in a Finnish sample of preadolescents (32). Each of the seven pain areas (neck, upper and lower extremities, chest, upper back, lower back and buttock) was scored 0-4 with the total score ranging from 0 to 28 indicating increasing severity. The internal consistency of the scale was good (α= 0.75).

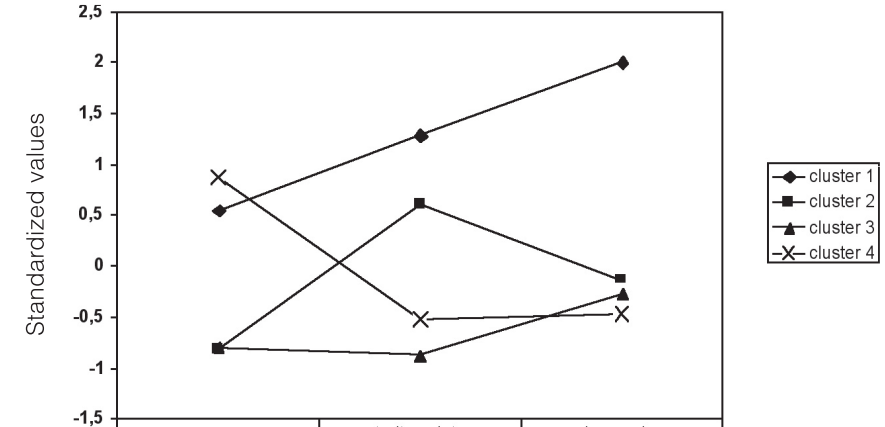
Somatic complaints: To measure the somatic symptoms of the children, the Child Behavior Checklist (CBCL) (33) was used. CBCL is a questionnaire for children/adolescents aged from 6 to 18. The reliability and validity of this questionnaire have been documented in Finland (34) as well as in many other countries. Altogether CBCL consists of 118 questions, each scored 0-2, from which one total behavior problem score can be summed. Higher values indicate increasing severity. In this study only the somatic complaints subscale was used. The somatic complaints score range from 0 to 22 and it includes the following items: nightmares, constipation, dizziness, tiredness, pain, headaches, nausea, eye problems, skin problems, stomach problems, vomiting.

Active joint count: An active joint was defined as a joint with swelling, or a limited range of motion with tenderness (35). Active joint count was assessed by a pediatric rheumatologist.

Ethics: The principles of the Declaration of Helsinki were followed. All patients and their parents received both oral and written information on the study and gave their written informed consent. The study protocol and procedures were accepted by the Ethical Committee of the Paijat-Hame Hospital District.

Statistical analysis

The preliminary screening of the relationships between variables gave only



	age	trait anxiety	depression
cluster 1	0,55	1,29	2
cluster 2	-0,81	0,61	-0,13
cluster 3	-0,79	-0,87	-0,27
cluster 4	0,87	-0,52	-0,47

Fig. 1. Presentation of the cluster groups according trait age, anxiety and depression. Cluster 1= teenagers scoring high in trait-anxiety and depression (n=20), Cluster 2= children scoring high in trait-anxiety and low in depression (n=43), Cluster 3= children scoring low in trait-anxiety and depression (n=28), Cluster 4= teenagers scoring low in trait-anxiety and depression (n=54). The trait anxiety and depression scores were measured by STAIC and CDI. The original values for the variables are reported in Table I.

few statistically significant associations in terms of linear relationships. Instead of additive components, associations based on combinatory elements seemed to have predominance in the material. We therefore chose to form types of cases based on age, trait-anxiety and depression. Both hierarchical and K-means cluster analysis were used to sort out such types which would come out repeatedly and be not too dependent upon the method and the initial values chosen. Since the variable trait-anxiety and depression correlated (r=0.689, p<0.001, n=145), we used the squared Mahalanobis distances in the calculations. The most stable classification came out with 4 clusters using k-means procedure with running means. Overall differences between the cluster groups regarding the duration of the disease, pain and somatic complaints were done using multivariate analysis of variance (MANOVA). Furthermore, differences between cluster groups were tested separately for each variable (duration of the disease, pain, functional disability and somatic complaints) by one-way-analysis of variance (ANOVA). Contingencies between the diagnoses and the cluster-group were studied by chi-square-test. Associations between the cluster groups and the children's self-efficacy were evaluated using multivariate analysis of variance (MANOVA). The analyses were done using SPSS 14.0 for Windows (36). A few missing values which seemed to be missing at random (MAR), were multiple imputed prior to the analyses by the Norm-program's data-augmentation procedure (37). Iteration was carried out in 2000 cycles; each 500th cycle produced one imputed matrix. Initial estimates were gained by the expectation-maximization (EM) method (38, 39).

Table I. Presentation of the clusters and the categorizing variables in children with JIA.

	Mean (SD)	Min	Max	N
Age				
Cluster 1*	13.16 (1.99)	8.40	15.70	20
Cluster 2	10.10 (1.49)	7.50	13.90	43
Cluster 3	10.17 (1.20)	8.00	12.30	20
Cluster 4	13.84 (0.96)	11.90	15.70	54
Anxiety				
Cluster 1	19.46 (4.50)	11.70	30.10	20
Cluster 2	15.05 (4.49)	8.00	26.00	43
Cluster 3	5.4 (3.36)	0.00	13.00	28
Cluster 4	7.63 (4.27)	0.00	16.70	54
Depression				
Cluster 1	13.98 (3.76)	8.60	22.00	20
Cluster 2	4.28 (2.87)	0.00	12.00	43
Cluster 3	3.64 (3.37)	0.00	11.00	28
Cluster 4	2.70 (2.12)	0.00	7.00	54

*Cluster 1: teenagers scoring high in trait-anxiety and depression; Cluster 2: children scoring high in trait-anxiety and low in depression; Cluster 3: children scoring low in trait-anxiety and depression; Cluster 4: teenagers scoring low in trait-anxiety and depression.

Results

In the whole sample the functional disability score mean (CHAQ) of the children was 0.3 (SD=0.4), the number of active joints mean was 1.7 (SD=3.2), the number of somatic problems mean was 3.9 (SD=2.7) and the frequency of pain mean was 3.7 (SD=4.3).

In order to determine whether the children could be grouped distinguishably, the K-means cluster method was applied to perform the classification of the children. The following set of variables was chosen as categorizing variables: trait-anxiety, depression and age. After exploring several cluster solutions, a 4-cluster solution (Fig. 1) was obtained, in which the clusters centroids differed from each other (Wilk's lambda=0.071, F=73.87, df1=9, df2=338.44, p<.001). The cluster means of categorizing variables differed significantly: age (F=84.50, df1=3, df2=141, p<0.001), trait-anxiety (F=66.39, df1=3, df2=141, p<0.001) and depression (F=80.08, df1=3, df2=141, p<0.001). The number of patients in each cluster was: Cluster 1 n=20, Cluster 2 n=43, Cluster 3 n= 28, Cluster 4 n=54. The descriptive statistics for the categorizing (cluster) variables are presented in Table I. The cluster groups so detected were named: teenagers scoring high (compared to the other cluster-groups) in trait-anxiety and

depression (1), children scoring high in trait-anxiety and low in depression (2), children scoring low in trait-anxiety and depression (3), and teenagers scoring low in trait-anxiety and depression (4).

The differences in the clinical parameters between the cluster groups were then investigated. Overall significant differences were found between the cluster groups (Wilk's lambda=0.691; F=3.61, df1=15, df2=378.60, $p<0.001$). When the cluster groups were investigated separately regarding each clinical parameter (Table II) the groups differed significantly in disease duration (F=3.77, df1=3, df2=141, $p=0.012$), pain (F=5.60, df1=3, df2=141, p=0.002), functional disability (F=5.00, df1=3, df2=141, $p=0.003$) and somatic complaints (F=6.35, df1=3, df2=141, $p<0.001$). Cluster 1 (teenagers with a high level of depression and trait-anxiety) had the highest rate of pain, highest disability rate and highest active joints counts compared to the other clusters. Cluster 4 (teenagers scoring low in trait-anxiety and depression) had the longest duration of the disease, the best disability rate and a low count of active joints. However, this cluster reported considerable pain. Clusters 2 and 3 comprised the younger groups with a mean age of 10 years. Cluster 2 (with low levels of depression but high in trait-anxiety) displayed a fairly high level of pain, but the lowest active joint count of the groups and the duration of the disease was the shortest. Cluster 3 (scoring low in both trait trait-anxiety and depression) also had the lowest level of pain and a low level in functional disability. However, the active joint count was fairly high (Table II). Regarding active joint count the difference between the clusters was not significant. However, a clear tendency could be seen. In order to detect the real effect, Clusters 2, 3 and 4 were contrasted to Cluster 1. Cluster 1 scored significantly higher on joint inflammation than the other groups combined (t=2.17, df=141, $p=0.032$). An interesting feature was discovered regarding the diagnosis. Diagnoses of oligoarthritis, oligoextended and polyarthritis were found in all four clusters (Table III).

Finally, it was analyzed how self-efficacy was related to these cluster-groups. Of the three self-efficacy factors (CASEsom, CASEpsych CASEsoc), all patients had the lowest score of self-efficacy in psychological functioning whereas self-efficacy in social functioning reached the highest level (Fig. 2). Cluster 1 had the lowest values in all the factors (CASEsom, CASEpsych, CASEsoc) whereas the strongest somatic, psychological and social self-efficacy was found in Cluster 3. The overall level between the groups was significant (Wilk's lambda=0.708, F= 5.73, df1=9, df2=338.44, $p<0.001$), differences taken separately were also significant p<0.001 in all the three variables. Effect sizes ranged from 0.11 to 0.18 measured by classical eta-square being from moderate to large according to Cohen's (40) classification. The observed power varied between 0.97 and 0.99.

Table II. Presentation of the clusters and disease-related parameters in children with JIA.

	Mean (SD)	Min	Max	*p*
Duration of disease				= 0.012
Cluster 1*	5.76 (4.10)	0	12.00	
Cluster 2	5.26 (2.51)	1	12.00	
Cluster 3	5.39 (3.05)	0	14.00	
Cluster 4	7.40 (4.08)	0	13.00	
Pain				= 0.002
Cluster 1	6.50 (4.63)	0	15.00	
Cluster 2	3.67 (3.94)	0	14.00	
Cluster 3	1.71 (2.80)	0	19.00	
Cluster 4	3.84 (45.73)	0	16.00	
CHAQ				= 0.003
Cluster 1	0.46 (0.48)	0	1.50	
Cluster 2	0.35 (0.49)	0	1.10	
Cluster 3	0.18 (0.25)	0	1.80	
Cluster 4	0.14 (0.27)	0	1.50	
Active joint count				= 0.114
Cluster 1	3.12 (4.52)	0	19.00	
Cluster 2	1.11 (1.75)	0	7.00	
Cluster 3	1.87 (3.99)	0	20.00	
Cluster 4	1.42 (2.92)	0	16.00	
Somatic complaints				= 0.000
Cluster 1	5.80 (3.04)	0	13.00	
Cluster 2	4.32 (2.60)	0	11.00	
Cluster 3	2.95 (2.48)	0	10.00	
Cluster 4	3.34 (2.29)	0	10.00	

*Cluster 1: teenagers scoring high in trait-anxiety and depression; Cluster 2: children scoring high in trait-anxiety and low in depression; Cluster 3: children scoring low in trait-anxiety and depression; Cluster 4: teenagers scoring low in trait-anxiety and depression. The probability value *p* refers to the difference between the cluster groups under each variable.

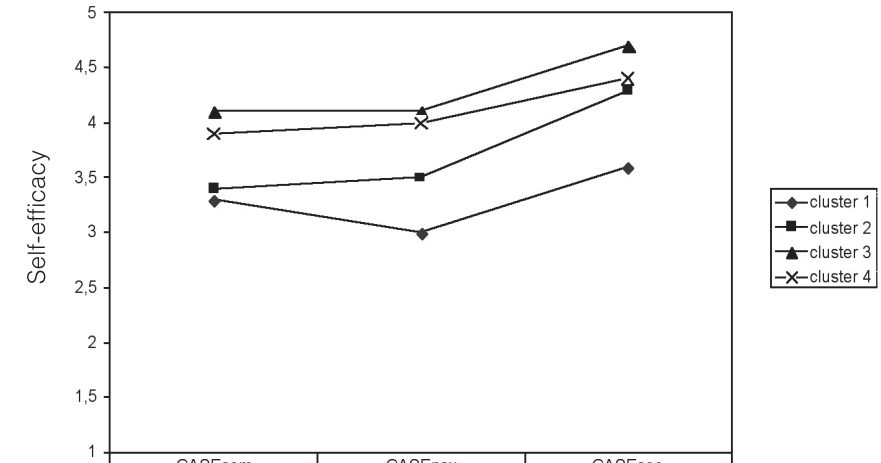
Table III. Diagnosis within the cluster groups*.

	Oligo	Extended oligo	Poly	Total
Cluster 1	8 (40%)	3 (15%)	9 (45%)	20 (100%)
Cluster 2	15 (35%)	10 (23%)	18 (42%)	43 (100%)
Cluster 3	10 (36%)	5 (18%)	13 (46%)	28 (100%)
Cluster 4	14 (26%)	7 (13%)	33 (61%)	54 (100%)

*non-significant.

Discussion

Studies regarding JIA in Sweden (4, 41) show that the children were clearly affected by their arthritis. However, the disability indexes in their studies were noticeably higher compared to our sample (41). The starting point for the current study was to cluster the patients based on depression and anxiety and not based on clinical parameters. Four distinguishable cluster groups were obtained with varying levels of anxiety



	CASEsom	CASEpsy	CASEsoc
cluster 1	3,3	3	3,6
cluster 2	3,4	3,5	4,3
cluster 3	4,1	4,1	4,7
cluster 4	3,9	4	4,4

Fig. 2. Association between the cluster groups and self-efficacy. Cluster 1: teenagers scoring high in trait-anxiety and depression (n=20); Cluster 2: children scoring high in trait-anxiety and low in depression (n=43); Cluster 3: children scoring low in trait-anxiety and depression (n=28); Cluster 4: teenagers scoring low in trait-anxiety and depression (n=54). Overall difference between the groups was significant (p<0.001).

and depression. Furthermore, we found a pain pattern which was not necessarily related to the severity of the disease or to the diagnosis (polyarticular, extended oligoarticular and oligoarticular diseases). In general, according to our results, the Finnish children with JIA are doing fairly well both clinically and psychologically, which was also reflected in a fairly high self-efficacy across all self-efficacy factors (somatic, psychological and social). One important factor contributing to this result is efficient medical treatment and interdisciplinary rehabilitation in locally concentrated treatment centers.

Summary of the findings

When the four cluster groups were analyzed against clinical parameters and self-efficacy, new information was obtained on their relationships. The most important finding was that in the cluster groups with highest levels of anxiety and depression (groups 1 and 2) self-efficacy was low, whereas in the groups with a lower level of anxiety and depression (groups 3 and 4), self-efficacy was high. In the groups in which self-efficacy was high and anxiety/depression was low, some medical parameters were quite good (pain, active joint count, somatic complaints). These results might indicate that self-efficacy regulates anxiety/depression and clinical parameters in a manner such that good self-efficacy helps the patients deal with their pain and disease activity, thus lowering their level of anxiety and depression. In cluster 3 with the highest self-efficacy disease activity was fairly high, but the children of the group did not suffer pain and trait-anxiety. In Cluster 1 lower self-efficacy might contribute to anxiety/depression, which might be related to pain and somatic complaints.

In Cluster 4 (teenagers scoring low in trait-anxiety and depression) the structure of the relationships between the variables is more complicated. This might partly to be explained by the age of the patients. Adolescents have a better ability to conceptualize pain. They also have a deeper understanding of the potential effects of arthritis and they are more prepared to express pain in self-reports than younger children (3, 42, 43). However adolescents are often expected to manage their disease with less parental support and they also face challenges of growth towards independence and consolidation of identity (44).

As a whole, the pattern of psychological well-being did not correspond with diagnosis, which concurs with previous studies (3, 45, 46). Thus we cannot assume that child's adjustment difficulties could be eliminated by medical treatment of the disease symptoms. Instead, children with JIA seem to form subgroups with some of them having risk for an unfavorable adaptation to their disease and life situation. It might expected that in this sample the cluster groups predisposed to pain chronification were groups 1 and 2, because their self-efficacy was low which aggravates pain, anxiety and depression.

In the whole sample, self-efficacy did not increase chronologically by age. One way to explain this is the nature of adaptation, which has to be seen as a two-way process and as a dynamic interplay between a person's traits and the current challenges (47) at hand, rather than a question of age and learning. Further analyses are needed to clarify the direction of the variables' associations and to describe precisely the role of disease-related self-efficacy in children with JIA. Trait-anxiety and depressive symptoms may also be a consequence of having chronic pain rather than the primary cause of the pain (48) and may also relate to lack of parental support (49). When studying depression and anxiety in relation to chronic disease it is important to bear in mind that depression and anxiety can stem from other sources than the disease. Therefore, all results should be interpreted with caution. A limitation of this study relates to the scales used: when measuring coping by generic scores of well-being, such as CHAQ, there is always a risk that measures used overlap with the psychological scales. To avoid this, we also used scales measuring purely somatic aspects of the disease.

Despite the fact that the levels of trait-anxiety and depression were fairly low in this sample, they were associated with pain and somatic complaints. Regarding anxiety, a frequent temporal sequence has been noted as "anxiety first and then subsequently depression" (50, 51). Depressive symptoms predict future child-reported pain in JIA (52). Thus being able to identify anxiety symptoms might help in the prevention of future depressive episodes and pain chronification.

Clinical implications

A clinical implication of our study is that it emphasized the importance of a multidimensional approach to pain and well-being in children with JIA. Due to the large sample size we think that our findings can be generalized to the population of JIA in Scandinavian countries, where the treatment protocols are corresponding and concentrated to specialized centres. In conclusion, clustering our patients helped to reveal the fact that trait-anxiety and depression occur to some degree in some of the children with JIA and that there is not necessarily a straight correspondence between clinical parameters, trait anxiety and depression. Self-efficacy seems to mediate this relationship.

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