Pediatric RESEARCH

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SYSTEMATIC REVIEW

Physical activity and sedentary levels in children with juvenile idiopathic arthritis and inflammatory bowel disease. A systematic review and meta-analysis

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BACKGROUND: Physical activity (PA) is essential for children throughout their growth and maturation. It improves physiological and psychological health and limits the risk of developing metabolic disorders. However, some chronic physiological and metabolic diseases may lead to decreased PA. The diversity of outcomes in the literature offers no consensus for physical activity and sedentary levels in children with juvenile idiopathic arthritis (JIA) or inflammatory bowel disease (IBD).

METHODS: A literature review and a meta-analysis were carried out with original studies from a Medline database search. Only high-quality studies (STROBE checklist) written in English comparing PA level or sedentary behavior (SB) between children with the disorders and their healthy peers were considered. The aim was to examine PA and SB in children with JIA or IBD compared to their healthy peers.

RESULTS: The literature review and meta-analysis identified decreased PA and increased time spent in SB in these populations, which may exacerbate both their lower physical fitness and the symptoms of their health disorders.

CONCLUSION: Results nevertheless show discrepancies due to the different materials and methods used and the variables measured. Further studies are needed to establish a gold standard method for assessing PA level in these populations.

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) and inflammatory bowel disease (IBD) such as Crohn's disease (CD) or ulcerative colitis (UC) are among the most common immune-mediated inflammatory diseases affecting the pediatric population. JIA encompasses seven rheumatoid diseases that appear before the age of 16 years, characterized by an overproduction of inflammatory cytokines at the joint level, leading to a chronic inflammatory state and regular painful crises. The prevalence of JIA was 44.7 in 100,000 children in the USA in 2009[1] and 32.6 in 100,000 children in Europe in 2010.[2] IBD is characterized by chronic inflammation located in the gastrointestinal tract, leading to painful injury (obstructions, fistulae, abscesses, etc.). Epidemiological data show that juvenile onset of IBD occurs in 25% of patients worldwide, with 18% of cases appearing before age 10 years.[3,4] Epidemiological data also point to a continual increase in the incidence of IBD in young people.[5,6]

JIA and pediatric IBD profoundly affect the physical, mental, social, and functional aspects of life, resulting in drastically decreased quality of life and physical fitness, and a negative impact on growth.[7–9] With the onset of the disease, children and adolescents are faced with a challenging new way of living, often with a cluster of disabling symptoms referred to as "sickness behavior," including pain, fatigue, and disturbed sleep. For instance, the study of Rashid et al. found that 50.2% of children with JIA reported consistently low pain, and 17.9% reported consistently high pain.[10] It has also been shown that, in young people with IBD, recurrent bouts of spasmodic abdominal pain and bloody diarrhea are very common.[11,12] Fatigue is also widespread in cases of both JIA and IBD. For instance, almost 75% of children with JIA complain of fatigue,[13] with one third of them describing moderate to severe levels,[14,15] and adolescents with IBD exhibit more fatigue than their healthy counterparts.[16] To cope with these challenging pathological conditions, some healthcare practitioners, family, and children themselves have tended to preclude physical activity (PA), fearing that it will worsen the symptoms of pain and fatigue.

PA is defined as any bodily movements produced by the skeletal muscle that result in energy expenditure.[17] The beneficial effect of PA in subjects with IBD and JIA has been praised for the potential regulatory effect of exercise on the balance between pro- and anti-inflammatory responses.[18,19] However, differences among studies in design and sample composition, disease activity, treatments used, and methods of assessment (objective or subjective) lead to divergent results on PA levels in children with these diseases.

We analyzed PA level in children and adolescents with JIA or IBD, paying special attention to methodological weaknesses that

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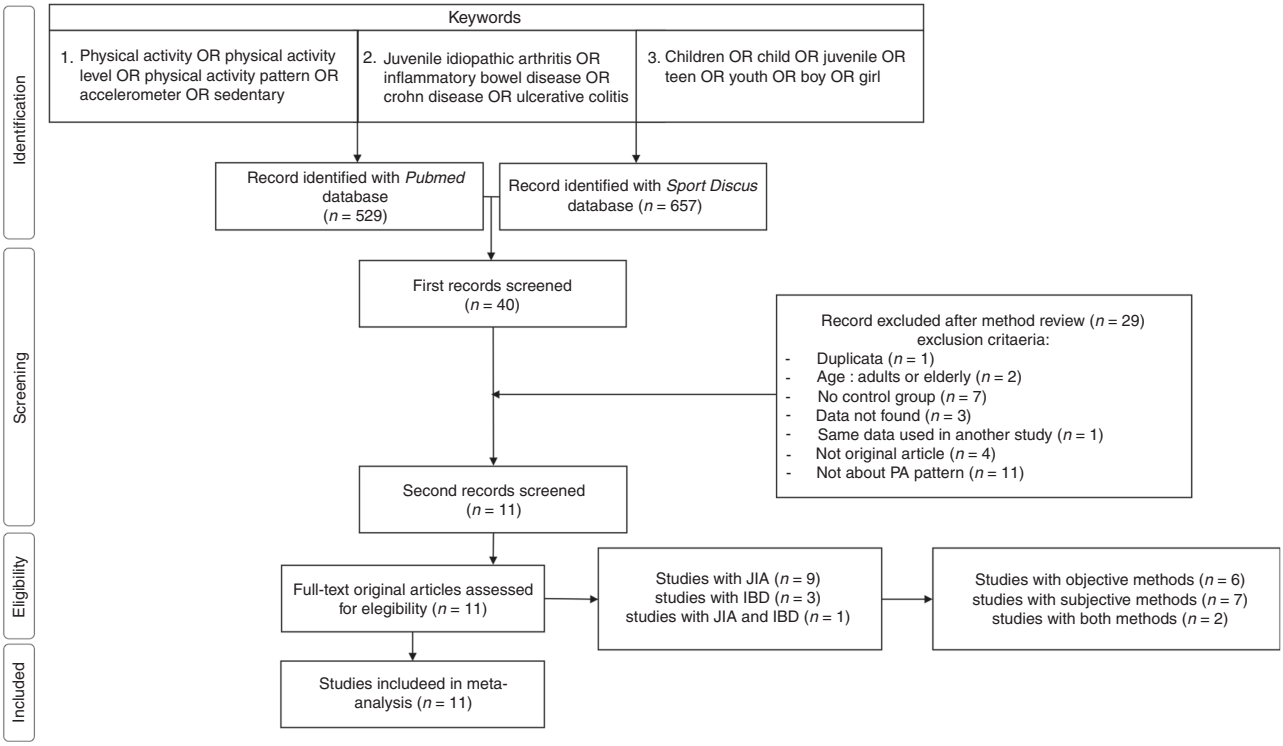

Fig. 1 Study selection following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) method

should be avoided in future studies in a review and meta-analysis. Our meta-analysis examined the variations in measurement methods. We hypothesized that children with JIA or IBD would be less active and more sedentary than their healthy peers.

MATERIALS AND METHODS

Inclusion and exclusion criteria

Participants. Participants included in the studies were children or teenagers diagnosed with JIA or IBD and healthy age- and sex-matched children. All participants were aged <18 years. Studies assessing adults or elderly people were excluded from the meta-analysis.

Type of studies and outcome measurement. Case–control, cross-sectional, and cohort studies that analyzed the difference in PA level and sedentary behaviors between children with JIA or IBD and healthy peers between January 1995 and September 2018 were included in this study.

Studies included the presentation of mean and standard deviations (SDs) of PA level and sedentary behaviors. Studies using subjective methods (diaries, questionnaires, self-reported time spent in moderate or vigorous physical activity (MVPA), or sedentary behaviors) and an objective method (accelerometry) were included. Literature reviews and meta-analysis were excluded.

The delta of mean data was calculated to make forest plots.

Search strategy to identify relevant studies

All the studies originated from MedLine (PubMed database), following the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[20] (Fig. 1).

Study selection. Relevant keywords were selected according to the population (1), pathology (2), and the variables measured for PA level (3). Studies were found with combined keywords containing "children," "child," "teen," or "youth" (1); "juvenile idiopathic arthritis," "juvenile arthritis," "inflammatory bowel disease," "Crohn's disease," or "ulcerative colitis" (2); and "physical activity," "physical activity level," "accelerometry," or "sedentary" (3). These were screened to select relevant studies according to their title. These in turn were screened based on their abstracts read by two independent reviewers. Finally, studies used in the selected articles were screened using the same method.

Risk of bias assessment. To avoid the risk of bias, all studies were submitted to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.[21]

Data extraction

Data from the selected studies were extracted using a standardized eligibility criteria sheet. Any discrepancy at this final stage was discussed among the reviewers, with an independent reviewer being consulted if a consensus could not be reached. Authors of papers were contacted where data were incomplete or needed further clarification. Data relating to general study information (authors, year of publication, sample size), study design (cross-sectional or cohort studies), participant characteristics (age, pathology), and results (mean and SD of PA level or sedentary parameters) were collected in a table (Table 1). For the studies that included a range of values, SDs were calculated.

When values were missing, the corresponding author was asked for clarification. In the absence of a response, incomplete studies were excluded.

Statistical analysis

After extraction, the data were compiled using the software designed specifically for meta-analyses (Comprehensive Meta-Analysis, version 2; Biostat, Englewood, NJ). For descriptive analyses, data were presented as mean and SD or median and interquartile range, according to statistical distribution. The Hedges' standardized mean differences were calculated using a random-effects model (DerSimonian and Laird approach) that

Table 1. Studies assessing PA level in children with JIA or IBD and teen

Study (author, year)	Country	Disorder	Sample: number of subjects, age (mean ± SD)	Design	Main findings
Armbrust et al. (2016)[36]	Netherlands	JIA	80 subjects, 8–13 yo	Fatigue and perceived health were assessed by questionnaire (respectively, PedsQl-MFS and CHAQ) and PA level by accelerometers (*Artical*) over 7 days	60% of patients with JIA suffered from daily low-energy levels; 27% suffered from very low-energy expenditure more than half the week. Low energy levels were best predicted by disability and low physical activity and were correlated with high fatigue
Bohr et al. (2015)[25]	Denmark	JIA	133 subjects, 7–20 yo (14 ± 3.37) and 1692 control (sex- and age-matched)	Disease activity and perceived health was assessed by questionnaire (respectively, JADAS and CHAQ) and PA level by accelerometers (*ActiGraph GM1T*) over 3–7 days	Significantly lower PA levels are shown in patients compared to controls. Patients with active disease are less active than patients without active disease
Bos et al. (2016)[37]	Netherlands	JIA	76 subjects, 8–13 yo (10.0 ± 1.4) and 131 controls (10.4 ± 1.2)	Diary to record PA level and sedentary time over 7 days	Children with JIA had a significantly lower PA level. They spent less time in moderate or vigorous PA and had a significantly higher mean time spent in sedentary activities compared to controls
Cavallo et al. (2015)[22]	Canada	JIA	107 subjects, 8–17 yo (12.8 ± 2.7) and 20 controls (12.9 ± 3.4)	Questionnaire to assess leisure activity time (CAPE) during the last 4 months	Children and adolescents with JIA tend to spend more time in sedentary behavior. Greater disease activity may dissuade children and adolescents from participating in more active pursuits
Gueddari et al. (2014)[45]	Morocco	JIA	50 subjects, 8–17 yo (11.5 ± 3.3) and 50 control (10.5 ± 3.8)	Diary to record PA level per day (each hour for 24 h). Disease activity and perceived health was assessed by questionnaire (JADAS and CHAQ, respectively)	The JIA group spent more time in bed and less time on moderate to vigorous PA than the control group. Patients with active disease are less active than patient without active disease
Henderson et al. (1995)[26]	Ohio (USA)	JIA	23 subjects, 5–11 yo and 23 control (sex- and age-matched)	PA level and sleep was measured for 3 days (minimum of 1 weekend day) using simultaneously accelerometers (*Caltrac*), and diary	There was less daily physical activity by this group of JRA patients than for healthy age- and sex-matched control subjects
Hulsegge et al. (2015)[46]	Netherlands	JIA	28 subjects, 7–15 yo (11.3 ± 2.4) and 2750 control, 6–10 yo	Questionnaire (APARQ) to assess PA level	JIA tend to be less physically active than healthy peers
Lelieveld et al. (2008)[23]	Netherlands	JIA	30 subjects, 16–18 yo (17 ± 0.6) and 106 control, 16–18 yo (16.7 ± 0.9)	Energy expenditure and PA level were assessed with a 3-day activity diary	Energy expenditure and PA level were significantly lower in the JIA group. The JIA group spent more time in bed and less time on moderate-to-vigorous PA. Only 23% of the JIA patients met public health recommendations to perform >1 h daily moderate-to-vigorous PA compared with 66% in the reference group
Limenis et al. (2014)[28]	Canada	JIA	50 subjects, 11–18 yo (median = 15)	Questionnaires to assess the PA level (PAQ-C and PAQ-A, respectively, for children and teens)	Children with JIA report significantly less activity than healthy children based on PAQ scores, with physical activity declining throughout adolescence
Maggio et al. (2010)[35]	Switzerland	JIA	31 subjects, 5 to 18 yo (10.8 ± 0.5) and 85 control (10.1 ± 0.3)	PA was assessed by accelerometers (*ActiGraph MT* 6471) over 7 days (periods from 8:00 am to 9:00 pm were analyzed)	JIA patients have lower PA level than controls
Mählmann et al. (2017)[4]	Switzerland	IBD	22 subjects (8 in active disease and 14 in remission), respectively, 14.69 ± 3.25 and 13.23 ± 2.96 yo, and 24 control, 12.38 ± 3.24 yo	Steps/day and sitting time was assessed by accelerometer (*FitBit*) over 5 consecutive days	Children with an active disease are less active than children in remission. Both IBD groups have a lower PA level than controls
Nørgaard et al. (2016)[47]	Denmark	JIA	61 subjects, 10–16 yo (13.3 ± 1.1) and 2055 control	Daily free-living PA was monitored with an accelerometer (*ActiGraph GT1M*) over 7 days	Children with JIA are less physically active than their age- and gender-matched healthy peers despite good disease control

Table 1 continued

Study (author, year)	Country	Disorder	Sample: number of subjects, age (mean ± SD)	Design	Main findings
Tarakci et al. (2011)[48]	Turkey	JIA	52 subjects, 8–17 yo (12.13 ± 2.92) and 48 control (11.27 ± 1.59)	Physical activity level and energy expenditure were assessed with a 1-day activity diary	The JIA group spent significantly less time in physical activity and showed a decrease in energy expenditure compared with the control group
Walker et al. (2015)[24]	Canada	JIA; CD	11 subjects with JIA (13.7 ± 2.4); 15 subjects with CD (15.0 ± 2.5) and 29 control (sex- and age-matched)	Sedentary time was assessed by accelerometer (*ActiGraph GT1M* and *GT3*) over 7 days, and sedentary behavior was assessed by self-administered questionnaire (TV hours/day) over 24 h	There were no differences between children with a chronic disease and controls in sedentary time or in the prevalence of TV watching and computer or video game usage for varying durations.
Werkstetter et al. (2012)[49]	Germany	IBD	39 subjects, 8–19 yo (15.1 ± 2.9 years) and 39 control (sex- and age-matched)	PA was assessed by accelerometer (*SenseWear Pro*) over 72 h (2 weeks days + 1 day at the week end)	The differences in duration of physical activity and number of steps between patients and controls did not reach significance. However, a strong trend was noted especially for a reduced duration of high-level physical activity in patients and also for the number of steps

PA physical activity, *JIA* juvenile idiopathic arthritis, *IBD* inflammatory bowel disease, *CD* Crohn's disease, *yo* years old

accounts for true variation in effects occurring from study to study and for random errors within one study.

In other words, to address the non-independence of data due to study effects, a random-effects model was used in preference to a fixed-effect one, because certain experimental variables showed wide variation. The I^2 index was used to measure heterogeneity, with 25, 50, and 75% indicating low, moderate, and high heterogeneity, respectively. Finally, an Egger test and funnel plots were used to assess publication bias. In the absence of bias, studies were distributed evenly around the mean effect size because of random sampling error. A p value of <0.05 was considered statistically significant.

RESULTS

Identification and selection of relevant studies

Study data that met our search criteria obtained before reduction steps were carried out are listed in Table 1. Of the 15 studies presented in the literature review, only 11 were included in the meta-analysis. Data were not available for two studies, and two studies did not compare the data obtained in JIA and IBD groups with healthy controls.

For this meta-analysis, the mean score of the quality of studies (STROBE checklist) was 19.00±1.33/22. The quality of studies selected for the meta-analysis was good, and all these studies were included in the meta-analysis.

Systematic review of the PA level and sedentary behaviors of children with JIA or IBD

The level of PA was lower in sick children than in their healthy counterparts. In the studies presented in Table 1, both subjective and objective methods show a trend toward decreased PA in children with JIA or IBD. Questionnaires and diaries show that children with JIA or IBD report less time spent in PA regardless of its intensity (low, moderate, or vigorous) with a particular decrease in MVPA, together with an increased time spent in sedentary behaviors (such as watching television or using a computer).[22] These results support the assertion that only 23% of the pathological pediatric population meet the public health recommendation in terms of PA (at least 1 h of MVPA per day) compared to 66% of healthy children.[23] However, most of the studies presented in this review assessed PA level in children with JIA, and fewer studies assessed it in children with IBD. Despite scant studies, similar results were found for both JIA and IBD.[24] Studies that assessed levels of PA relative to disease activity found that children with active disease had a lower PA level than children in remission,[4,25] suggesting that the activity of the disease was the main deterrent to PA for these children. All the studies showed similar results for PA level. As regards sedentary behaviors, consensus in the data is less clear, although levels of sedentary behaviors seem to be increased in children with JIA or IBD.

Meta-analysis comparing PA level and sedentary behavior between children with JIA or IBD and healthy children

Different methods are used to assess PA level, but no gold standard exists. Although objective methods help to eliminate the methodological bias associated with patient subjectivity, they cannot provide information about the nature of the PA. The meta-analysis showed that children with JIA or IBD are less active than their healthy peers. Results obtained by both objective and subjective methods (Fig. 2) present a decreased PA level in children with JIA or IBD. However, different results were obtained by Mählmann et al.[4] (studies 3ba and 3bb) and showed more time spent in vigorous PA. Results obtained by subjective methods (from study 6a to 10b) present weaker significance than those obtained by objective methods.

Results obtained by objective methods (from study 1 to 2cb) show a longer time spent in sedentary behavior in children with

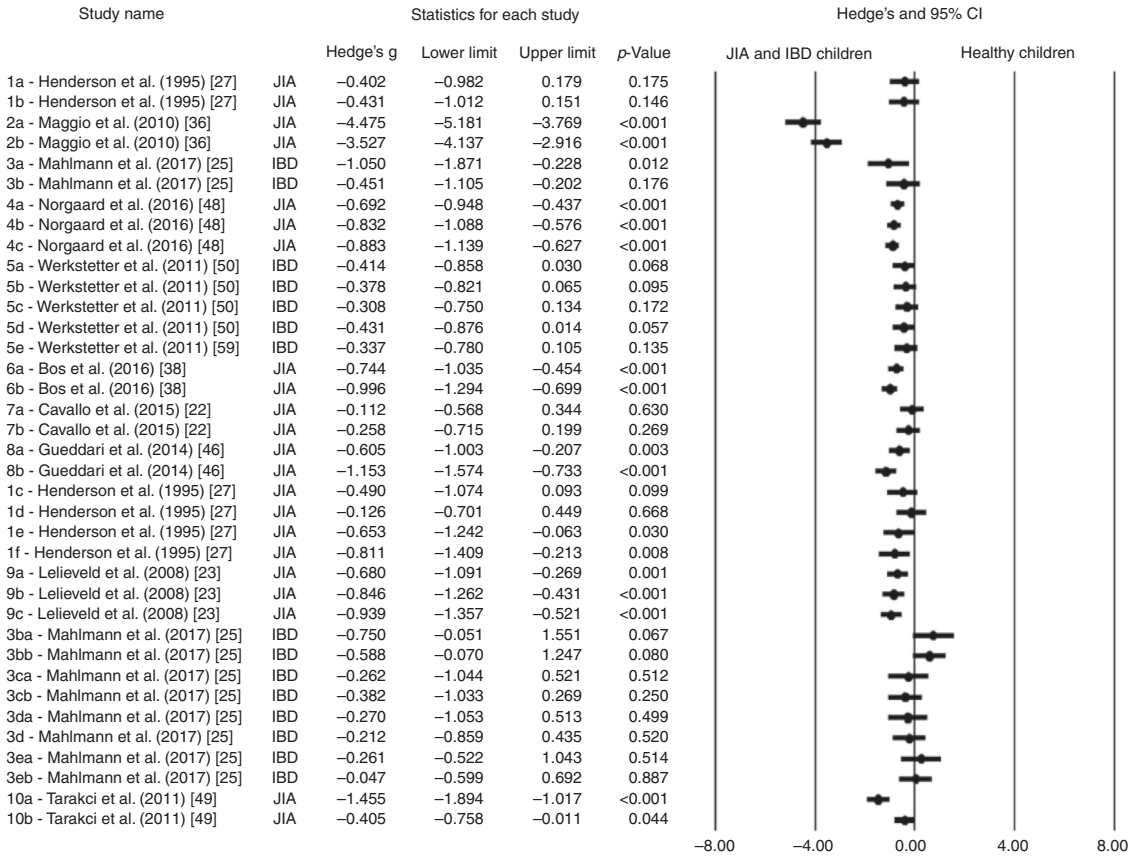

Fig. 2 Forest plots of physical activity level in juvenile idiopathic arthritis and inflammatory bowel disease children compared to healthy children assessed with objective and subjective methods

JIA and IBD compared to their healthy peers (Fig. 3). By contrast, sedentary behaviors present lower SDs when assessed with subjective methods (from Figs. 3 and 4b) than with objective methods. The *p* value is also lower for results obtained by subjective methods.

DISCUSSION

The aim of this literature review and meta-analysis was to analyze PA level in children and adolescents with JIA and IBD compared to their healthy peers. The results yield evidence that level of PA is lower and sedentary behaviors are higher in children with JIA or IBD compared to healthy children. However, the difference between means of pathological and control groups is not constant across studies, particularly according to the assessment method (i.e., subjective or objective). The meta-analysis enabled us to isolate subjective and objective methods. Results showed that a lower PA level was observed in children with JIA or IBD only when assessed with an objective method. The distribution and potential bias of the studies will now be discussed.

Results suggest that objective methods highlight greater differences in PA level between children with JIA or IBD and their healthy peers than do subjective methods. For a similar sample size, results obtained by objective methods highlight greater differences between pathological and control groups.[4,26] However, different sample sizes between studies and different SD values may explain the differences in results between studies. The heterogeneity of the results warrants discussion. The objective methods included in this meta-analysis used different models of accelerometer (*Caltrac*, *ActiGraph*, *Fitbit*, or *SenseWear Pro*), with measured variables expressed in quantitative or qualitative units, such as counts per minute (cpm), steps per day, daily energy expenditure (in kcal or MET), or time spent in different types of activity. Data has also been recorded for different periods of time (from 1 to 7 days). Studies include different numbers of subjects and sample sizes, contributing to the heterogeneity of results. Results obtained through the meta-analysis show that children with JIA or IBD are more sedentary than their healthy peers. For the assessment of sedentary behaviors, subjective methods seem to highlight larger differences, although overestimation or underestimation of children's PA participation must be taken into account.

Our study tells us nothing about mechanisms or reasons for the lower PA level reported in children with JIA or IBD. However, it has been suggested that an impaired immune profile, with a chronic inflammatory state, leads to pain and metabolic disorders. Chronic inflammation is known to promote muscle wasting and induce dysregulations in energy supply (such as difficulties with lipid oxidation). All these consequences tend to increase fatigue and decrease exercise tolerance. These mechanisms lock children with JIA or IBD into a vicious cycle that contributes to decreased PA[27] and is confirmed in our meta-analysis (Fig. 4). Inactivity is known for its negative effects on physiological and psychological health. These conditions may thus worsen symptoms and degrade physical fitness,[27] resulting in an increase in comorbidities, which may in turn have a long-term negative effect.

Mechanisms and consequences of pain

Liemenis et al.[28] stated that the activity of the disease is related to exacerbated pain or fatigue, which may contribute to reduced participation in PA. Fifty percent of children with rheumatic diseases suffer from musculoskeletal pain in several locations, sometimes accompanied by joint pain,[29] and 30–50% of children with IBDs experience accompanying abdominal pain.[30,31]

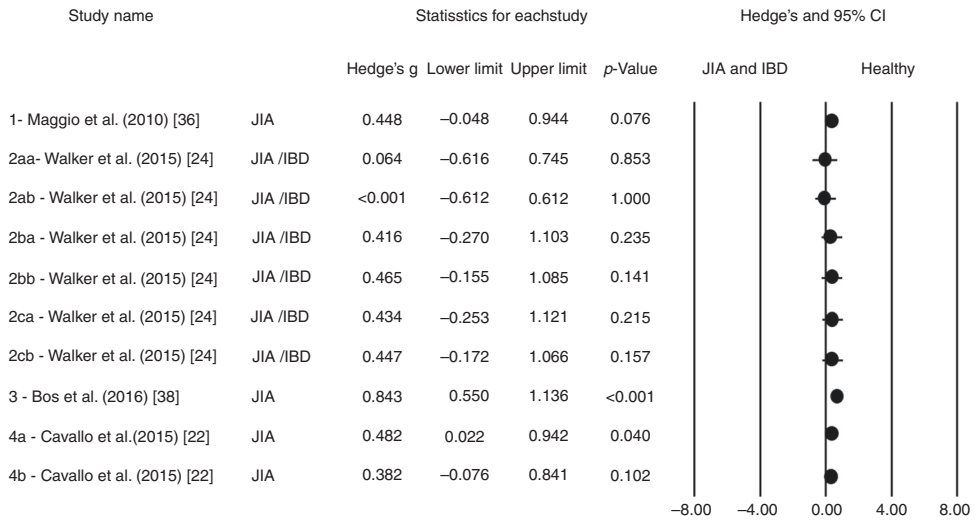

Fig. 3 Forest plots of sedentary behaviors in juvenile idiopathic arthritis and inflammatory bowel disease children compared to healthy children assessed with objective and subjective methods

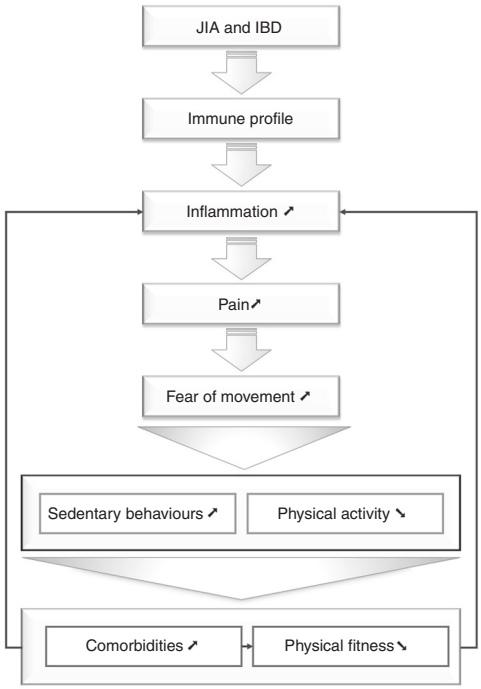

Fig. 4 Effects of juvenile idiopathic arthritis and inflammatory bowel disease on physical activity level, sedentary behaviors, and physical fitness

However, pain is often defined as a subjective sensation that depends on age, fatigue, or type and duration of disease and that may itself be affected by the disease,[32] which may explain the divergent results in the literature.

The effects of pain on children with JIA are numerous and involve the whole body. Biological factors have direct effects on pain by impairing mobility or by the action of pro-inflammatory entities on nociceptors. Unlike adults, children have a lower pain threshold, particularly due to a lack of pain experience and to the slow maturation of pain control mechanisms.[33] Pain is exacerbated in children with JIA by an acute inflammation produced in the joints.[34] Inflammatory entities produced in synovial joints adversely affect nervous afferent pathways and increase pain sensitivity by overstimulation. These mechanisms are similar to those induced in IBD. Musculoskeletal, joint, or abdominal pain induced by inflammation may often be increased by intense PA because of its inflammatory effect or impact. Soreness may therefore lead to avoidance of movement, initiating a deconditioning spiral that contributes to a decrease in PA level. Maggio et al.[35] indicate that the fear of movement is a greater deterrent in PA than the pain itself. Armbrust et al.[36] and Bohr et al.[25] found a positive correlation between pain and fatigue, and Bos et al.[37] found a negative correlation between pain and well-being. All these findings are correlated with low PA level and high level of sedentary behaviors, demonstrating that pain may contribute to decreased daily PA in children with health disorders.

Mechanisms and consequences of fatigue

These pathologies are characterized by high level of tumor necrosis factor (TNF)-alpha, which lead to decreased insulin sensitivity.[38] These metabolic disorders will impair metabolic flexibility, leading to prompter fatigue, and thereby to reduced exercise tolerance.

Inflammatory entities produced in these disorders (such as TNF-alpha) are known to be implicated as mediators in muscle wasting.[39] The decreased muscle mass may oblige children with JIA or IBD to use more energy than healthy children to generate the same strength level.[40] This overwork then leads to acute neuromuscular fatigue, amplifies generalized fatigue, and finally results in decreased PA level. Mechanisms of inflammation have many negative effects on the body, affecting central nervous system activity, and resulting in stress and depression linked to fatigue.[41]

These considerations may explain why sick children declare a higher energy expenditure and vigorous PA when assessed with a subjective method[4] (here, the International Physical Activity Questionnaire), regardless of disease status. These results may stem from lower physical fitness, which contributes to exacerbated fatigue during exercise and a consequent overestimation of the effort expended. Finally, decreased performance and depreciated self-worth, combined with an apprehension of pain (on the part of the medical and social environment, as well as the children themselves) lead to decreased participation in PA.[13,42]

More and more studies have been assessing the effects of different PA programs in JIA and IBD during therapies. The review by Catania et al.[43] and that of Narula and Fedorak[44] highlight beneficial effects of PA on symptoms of JIA and IBD, respectively.

These findings underline the need to increase PA level and limit sedentary behavior in this population.

CONCLUSION

Children with JIA or IBD are less active than healthy children and spend more time in sedentary behaviors. Generally, symptoms induced by JIA and IBD (mainly pain) contribute to decreased exercise tolerance and degrade physical fitness, decreasing PA level in children with JIA or IBD. However, specific attention needs to be paid to the design of studies that can tend to induce bias, especially for the assessment of PA. Objective methods are more robust in highlighting differences between sick and healthy populations, but they also are very heterogeneous because of the diversity of the variables and measurements used. Studies assessing sedentary behaviors do not show such a method-related effect. It might be useful to adopt an overall approach to the assessment of PA level using both objective and subjective methods to assess the quantitative and qualitative elements of PA level. Further research is needed to establish a gold standard method for assessing PA level for these population.

ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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