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Chapter 5

Physical activity in adolescents with juvenile idiopathic arthritis

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Abstract

Objective
To explore physical activity (PA) in adolescents with juvenile idiopathic arthritis (JIA) compared with a healthy population and to examine associations between PA and disease-related factors.

Methods
Total energy expenditure (TEE), activity-related energy expenditure (AEE), PA level, and PA pattern were assessed with a 3-day activity diary. Aerobic capacity was assessed using a Symptom Limited Bicycle Ergometry test. Functional ability was assessed with the Childhood Health Assessment Questionnaire. Disease activity was assessed using Paediatric Rheumatology International Trials Organisation core set criteria. Overall well-being was measured using a visual analog scale, and time since diagnosis was assessed by retrospective study from patients' charts. We used a cross-sectional study design. Reference data were collected from healthy Dutch secondary school children.

Results
Thirty patients and 106 controls were included (mean ± SD age 17.0 ± 0.6 and 16.7 ± 0.9 years, respectively). TEE, AEE, 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 hour daily moderate to vigorous PA compared with 66% in the reference group. Higher PA was associated with higher levels of well-being and maximal oxygen consumption.

Conclusion
Adolescents with JIA have low PA levels and are at risk of losing the benefits of PA. Low PA is not related to disease activity, and control over the disease does not restore previous PA levels. Interventions by pediatric rheumatologists are needed to increase PA levels in patients with JIA.
Introduction

The beneficial effects of physical activity (PA) on normal growth and development of children and adolescents have been widely recognized\(^1,2\). PA is needed to maintain optimal metabolic function and to prevent a number of chronic diseases\(^1\), and is essential for the social, emotional, and cognitive development of children and adolescents\(^3\). All of these benefits apply equally for children and adolescents with juvenile idiopathic arthritis (JIA); therefore, PA should be a goal in any comprehensive treatment program\(^4\). PA is determined by genetics, environment, and lifestyle\(^5\), and can be defined as a behavior that is characterized by any bodily movement that results in an increase in energy expenditure above the basal level\(^6,7\).

Some evidence reports that prepubertal children with JIA are less physically active when compared with healthy children\(^8\). Additionally, other evidence reveals that children with JIA have moderate to severe impairment in physical fitness, as expressed by low maximal oxygen consumption (VO\(_2\))\(^9\). Recent evidence shows that adolescents with JIA also have low aerobic and anaerobic fitness levels\(^10\).

Although the positive effects of PA on health and development have been recognized, the optimal intensities, volumes, and modalities are unclear\(^11\). PA guidelines for children and adolescents have been developed by several organizations and agencies, but very little evidence is available for a certain dose-response relationship or a particular threshold value from which guidelines can be obtained\(^12\). Recently, an expert panel under a contract with the Centers for Disease Control and Prevention formulated an evidence-based PA guideline for school-aged youth. School-aged youth should participate daily in \(\geq 60\) minutes of moderate to vigorous PA that is developmentally appropriate, enjoyable, and involves a variety of activities\(^13\).

Several techniques have been developed for measurement of PA and energy expenditure in children and adolescents\(^14,15\). Activity diaries are one of the methods used, and although their accuracy depends on the cooperation of the subjects, they show a number of advantages. Activity diaries do not need complicated technology and are inexpensive. They measure intensity, duration, and frequency of PA. PA can be expressed as PA level, PA pattern, and activity-related energy expenditure (AEE). PA level expresses the energy needs as multiples of the basal metabolic rate (BMR) and is the total energy expended (TEE) during a day.
divided by the BMR\(^{16}\). A compendium has been developed and is used to classify the energy costs of human physical activities\(^{17}\). BMR is the energy expended in order to sustain life in a resting individual\(^{16,18}\). AEE is expressed as \((0.9 \times \text{TEE}) - \text{BMR}\), assuming a diet-induced thermogenesis of 10\%\(^{19}\). PA pattern is determined by the duration, intensity, and frequency of a specific type of PA. Both a 3-day and a 7-day activity diary have proved to be reliable. The latter has been validated by use of the doubly-labeled water method, which is regarded as the preferred method for determining energy requirements of healthy and clinical populations\(^{20-22}\).

To our knowledge, PA has not previously been studied in adolescents with JIA. The aim of the present study was to explore PA in adolescents with JIA compared with a healthy age-matched population and to examine associations between PA and disease-related factors.

**Patients and methods**

**Patients**

Patients attending an adolescent JIA outpatient clinic were eligible for this study. Patients were diagnosed by a pediatric rheumatologist using International League of Associations for Rheumatology criteria\(^{23}\). The adolescent JIA clinic is a combined outpatient clinic of the Beatrix Children's Hospital and the adult rheumatology clinic of the University Medical Center Groningen, with the aim of transferring children ages 16-18 years with JIA from pediatric to adult care. This outpatient clinic was started in 2001 to improve care for adolescents with JIA. This study was designed to obtain more detailed information on the PA of these adolescents. Reference data for PA were collected from healthy Dutch secondary school children, because no published reference data for Dutch adolescents were available. A total of 315 students ages 16-18 years from 5 secondary schools in the northern part of The Netherlands were asked to fill in a 3-day activity diary, and height and weight were measured. Patients were fully informed about the use of the activity diary and informed consent was obtained.

We used a cross-sectional study design and included a patient group and a reference group. Weight and height were determined using an electronic scale and a stadiometer. Body mass index was calculated as body mass (in kg) / height\(^2\) (in meters).
**Activity diary**

PA was assessed with a 3-day activity diary. The patients and the reference group were asked to record their level of activity for 3 days (3 × 24 hours) in 1 week on a preprinted form. One of these days had to be a Saturday or Sunday. Every 15 minutes, the dominant activity had to be scored using a number from 1-9, where 1 = sleeping, resting in bed; 2 = sitting, eating, writing, etc.; 3 = standing, washing, combing, etc.; 4 = walking indoors (<4 km/hour), light home activities; 5 = walking outdoors (4-6 km/hour), housekeeping; 6 = recreational sport and leisure time activities with low intensity; 7 = recreational sport and leisure time activities with moderate intensity; 8 = recreational sport and leisure time activities with high intensity; and 9 = competition sport. Patients could contact the investigator or describe a type of activity on the form instead of giving a number if they were unsure. After completion, the form was sent by mail or it was collected. A PA ratio was allotted to each of the different 9 categories following the modification of Bratteby et al\(^{22}\). A PA ratio is the ratio of the energy expended by an individual in a particular category as multiples of BMR. To calculate TEE, all 15-minute periods of each category were summed, divided by 96, and multiplied by the PA ratio value of each category and the predicted BMR (BMRp), after which all categories were totaled\(^{22}\). The prediction formula according to Schofield was used\(^{24}\). BMRp for boys = 0.074 × body weight (in kg) + 2.754 MJ/day. BMRp for girls = 0.056 × body weight (in kg) + 2.898 MJ/day. PA level, AEE, and PA pattern (time spent in each category and time spent on moderate to vigorous PA) were calculated.

**Symptom Limited Bicycle Ergometry test**

Aerobic capacity was assessed using a Symptom Limited Bicycle Ergometry test, which was performed on an electronically braked cycle ergometer (Jaeger physio hc; Viasys, Bilthoven, The Netherlands). The seat height was adjusted to the patient's comfort. Rest was taken until all measured variables were stable. Cycling started at a workload of 0W and the workload was increased by 20W every minute until the patient stopped due to volitional exhaustion, despite strong verbal encouragement from the experimenters. Patients breathed through a mouthpiece that was connected to a calibrated metabolic cart (Oxycon pro, Jaeger; Viasys). Expired gas was passed through a flow meter, an oxygen analyzer, and a carbon dioxide analyzer. The flow meter and gas analyzer were connected to a computer that calculated breath-by-breath minute ventilation, \(V_O_2\), carbon dioxide production (\(V_C_O_2\)), and respiratory exchange ratio from conventional equations. \(V_O_2\), \(V_C_O_2\), and respiratory exchange ratio were recorded at 30-
second intervals. Heart rate was measured continuously during the maximal exercise test. VO₂ at maximal effort was recorded as VO₂peak.

Functional ability
Functional ability was assessed with the validated Dutch translation of the Childhood Health Assessment Questionnaire (CHAQ)²⁵,²⁶. In 8 domains (dressing/grooming, arising, eating, walking, hygiene, reach, grip, and activities), a number of questions were answered and scored on a scale of 0 to 3, where 0 = able to do with no difficulty, 1 = able to do with some difficulty, 2 = able to do with much difficulty, and 3 = unable to do. When assistance or aids were required for a domain, the score for that domain was raised to a minimum of 2. The time period for the self-assessment was a week. The mean of the 8 scores determined the CHAQ score (range 0-3). Cronbach's alpha ranged from 0.76-0.97 for the 8 domains²⁶.

Time since diagnosis
Time since diagnosis was assessed by retrospective study from patient's charts. Time since diagnosis was defined as the time period between time of disease onset and time of assessment.

Disease activity
Disease activity was assessed by an adult and a pediatric rheumatologist using the Paediatric Rheumatology International Trials Organisation core set criteria²⁷. Disease activity was accordingly classified as active disease, inactive disease, clinical remission receiving medication, and clinical remission not receiving medication. Active disease was defined as active arthritis in ≥ 1 joint. Inactive disease was defined as no signs of disease with medication. Clinical remission receiving medication was defined as 6 continuous months without active disease while receiving medication. Twelve months of not receiving medication and no signs of active disease was defined as clinical remission not receiving medication.

Overall well-being
Overall well-being was measured using a visual analogue scale (VAS) consisting of a 10 centimeter horizontal line with short vertical bars at each end. “Very well” was written at the left end (score of 0) and “very bad” at the right (score of 10). Patients were instructed to
indicate their overall well-being during the past week with a vertical line. Higher values equaled worse overall well-being.

Statistical analysis

SPSS software, version 14 (SPSS, Chicago, IL) was used for the statistical analysis. Descriptive statistics were used for patient and reference group characteristics, for TEE, AEE, BMR, and PA level, and for time spent at the different categories of PA. Independent sample t-tests were used to determine differences of patient characteristics, TEE, BMR, and PA level between the JIA group and the reference group data. Nonparametric Mann-Whitney U tests were used to determine differences in categories of PA between the JIA group and the reference group data. Spearman's correlation analyses were used to assess associations between disease-related variables and PA level. A correlation coefficient between 0.26 and 0.49 reflects poor agreement, those between 0.50 and 0.69 reflect moderate agreement, and those $\geq 0.70$ reflect high agreement. $P$ values less than 0.05 were considered statistically significant.

Results

Of the 37 patients present in our outpatient clinic, 36 were willing to participate in the study. Thirty-one patients returned their diaries (86% response rate). One diary was incomplete and was omitted. Therefore, 30 patients were included, 12 boys and 18 girls. The population consisted of 1 patient with systemic-articular JIA, 7 patients with oligoarticular JIA, 2 patients with extended oligoarticular JIA, 11 patients with polyarticular rheumatoid factor (RF)-negative JIA, 4 patients with polyarticular RF-positive JIA, 2 patients with psoriatic arthritis, and 3 patients with enthesitis-related JIA. Eight patients had active disease, 9 patients had inactive disease, 8 patients were in clinical remission, and 5 patients were in remission. One hundred fifteen of 315 students in the reference group returned their diaries (37% response rate). Nine diaries were not complete and therefore were omitted. A total of 106 subjects were included in the reference group. Patient and reference group characteristics are described in Table1. Independent sample t-tests showed no significant difference for age, height, weight, and body mass index between the JIA patients and the reference group.
Table 1. Characteristics of the JIA group and the reference group

|                      | JIA group (n = 30) | Reference group (n = 106) | P†  
|----------------------|--------------------|---------------------------|------
| Age, years           | 17.0 ± 0.6         | 16.7 ± 0.9                | 0.07 |
| Height, cm           | 173 ± 8            | 175 ± 9                   | 0.18 |
| Weight, kg           | 63.8 ± 13.4        | 63.4 ± 8.9                | 0.88 |
| Body mass index, kg/m² | 21.2 ± 3.3       | 20.7 ± 2.5                | 0.34 |
| CHAQ score (range 0-3) | 0.5 ± 0.5        |                           |      |
| VAS overall well-being (0-10 cm)‡ | 1.8 ± 1.8     |                           |      |
| Time since diagnosis, years | 8.0 ± 4.9     |                           |      |
| VO_{2peak} (liters × minute⁻¹) | 2.27 ± 0.62   |                           |      |
| VO_{2peak} (ml × kg⁻¹ × minute⁻¹) | 35.70 ± 7.45 |                           |      |

* Values are the mean ± SD. JIA = juvenile idiopathic arthritis; CHAQ = Childhood Health Assessment Questionnaire; VAS = visual analog scale; VO_{2peak} = peak oxygen uptake.
† Based on independent sample t-tests.
‡ 0 = high level of well-being; 10 = low level of well-being.

**TEE, AEE, calculated BMRp and PA level**

A significantly lower TEE, AEE, and PA level was found for both boys and girls in the JIA group compared with the reference group, as measured with independent sample t-tests (Table 2). No significant difference of BMRp was found for both boys and girls between the 2 groups. Boys in both groups had a significantly higher TEE and BMRp than girls. In the reference group, boys had a significantly higher AEE than girls. In the JIA group, boys also had a much higher AEE but the difference was not significant. No significant difference was found for PA level between boys and girls in both groups

Table 2. Independent sample t-tests between the JIA group and the reference group

|                      | JIA group (n = 30) | Reference group (n = 106) | P
|----------------------|--------------------|---------------------------|------
| TEE (MJ × day⁻¹)     | 12.17 ± 3.38       | 14.48 ± 3.38              | <0.01|
| Boys                 | 13.88 ± 3.71       | 16.50 ± 3.47              | <0.05|
| Girls                | 11.03 ± 2.67       | 12.99 ± 2.41              | <0.01|
| AEE (MJ × day⁻¹)     | 3.99 ± 2.20        | 6.12 ± 2.58               | <0.01|
| Boys                 | 4.52 ± 2.56        | 7.03 ± 2.94               | <0.01|
| Girls                | 3.64 ± 1.92        | 5.45 ± 2.05               | <0.01|
| BMRp (MJ × day⁻¹)    | 6.96 ± 1.20        | 6.91 ± 0.94               | 0.82 |
| Boys                 | 7.97 ± 1.04        | 7.82 ± 0.63               | 0.65 |
| Girls                | 6.28 ± 0.74        | 6.24 ± 0.41               | 0.81 |
| PA level (TEE/BMRp)  | 1.74 ± 0.29        | 2.09 ± 0.39               | <0.01|
| Boys                 | 1.72 ± 0.31        | 2.11 ± 0.41               | <0.01|
| Girls                | 1.74 ± 0.28        | 2.08 ± 0.37               | <0.01|

* Values are the mean ± SD. JIA = juvenile idiopathic arthritis; TEE = total energy expenditure; MJ = megajoule; AEE = activity-related energy expenditure; BMRp = predicted basal metabolic rate; PA = physical activity.
† 45 boys, 61 girls
PA pattern

Most time in both groups was spent on the 2 lowest categories: laying and sitting (Table 3). Adolescents in the JIA group spent significantly more time in bed than the reference group. The JIA group spent significantly less time in each of the 3 highest PA categories compared with the reference group. Only 23% of patients in the JIA group met public health recommendations to perform ≥ 1 hour daily moderate to vigorous PA compared with 66% in the reference group. The JIA group spent an average of 87 minutes/day on moderate to vigorous PA compared with 133 minutes in the reference group.

Table 3. Time spent (in hours) at the different categories of physical activity in the JIA group and the reference group, and P values by Mann-Whitney U test*

<table>
<thead>
<tr>
<th>Physical activity category</th>
<th>JIA group (n = 30)</th>
<th>Reference group (n = 106) †</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Sleeping, resting in bed</td>
<td>10.41 ± 2.03</td>
<td>9.02 ± 1.28</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>2. Sitting, eating, writing, etc.</td>
<td>8.38 ± 3.03</td>
<td>8.84 ± 1.79</td>
<td>0.73</td>
</tr>
<tr>
<td>3. Standing, washing, combing, etc</td>
<td>1.76 ± 1.06</td>
<td>1.90 ± 0.90</td>
<td>0.38</td>
</tr>
<tr>
<td>4. Walking indoors (&lt; 4 km/hour), light home activities</td>
<td>1.23 ± 1.05</td>
<td>1.21 ± 1.08</td>
<td>0.87</td>
</tr>
<tr>
<td>5. Walking outdoors (4-6 km/hour), housekeeping</td>
<td>0.77 ± 0.86</td>
<td>0.81 ± 0.68</td>
<td>0.39</td>
</tr>
<tr>
<td>6. Recreational sport and leisure time activities with low intensity</td>
<td>0.73 ± 1.13</td>
<td>0.52 ± 0.59</td>
<td>0.77</td>
</tr>
<tr>
<td>7. Recreational sport and leisure time activities with moderate intensity</td>
<td>0.29 ± 0.53</td>
<td>0.73 ± 0.77</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>8. Recreational sport and leisure time activities with high intensity</td>
<td>0.36 ± 0.49</td>
<td>0.61 ± 0.59</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>9. Competition sport</td>
<td>0.07 ± 0.18</td>
<td>0.36 ± 0.50</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

* Values are the mean ± SD. JIA = juvenile idiopathic arthritis.
† 45 boys, 61 girls

PA and disease-related factors

A significant inverse association was found between both PA level and AEE and VAS well-being (Table 4). A significant positive association was found between both PA level and AEE and time since diagnosis and between AEE and VO2peak. The association between PA level and VO2peak showed no significance. No association was found between PA level and AEE and disease activity and functional ability.
Table 4. Spearman’s correlation coefficient in the juvenile idiopathic arthritis group (n = 30)*

<table>
<thead>
<tr>
<th></th>
<th>VAS well-being</th>
<th>Time since diagnosis</th>
<th>Disease activity</th>
<th>CHAQ</th>
<th>Absolute $V_O^{2peak}$</th>
<th>Relative $V_O^{2peak}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA level</td>
<td>- 0.37†</td>
<td>0.46‡</td>
<td>0.16</td>
<td>- 0.11</td>
<td>0.30</td>
<td>0.13</td>
</tr>
<tr>
<td>AEE</td>
<td>- 0.49‡</td>
<td>0.54‡</td>
<td>0.30</td>
<td>- 0.22</td>
<td>0.55‡</td>
<td>0.24</td>
</tr>
</tbody>
</table>

* VAS = visual analog scale; CHAQ = Childhood Health Assessment Questionnaire; $V_O^{2peak}$ = peak oxygen uptake; PA = physical activity; AEE = activity-related energy expenditure.
† $P < 0.05$
‡ $P < 0.01$

Discussion

This study shows a significantly lower TEE, AEE, and PA level for adolescents with JIA compared with healthy controls. Only 23% of adolescents with JIA meet public health recommendations to perform 1 hour/day of moderate to vigorous PA compared with 66% in the reference group, as measured with a 3-day activity diary. Adolescents with JIA lay or sleep significantly more and are significantly less vigorously active than healthy controls. Most adolescents with JIA lack the benefits of PA. Low PA patterns developed in youth and adolescence are likely to persist in adulthood, resulting in a sedentary lifestyle.

Why then are adolescents with JIA less physically active than healthy peers? PA as a type of behavior, according to the social cognitive theory of Bandura, is multidimensionally determined within a dynamic interplay between individual agency and social structure.

Pender has used the social cognitive theory to explore factors and relationships contributing to PA (the health promotion model). Perceived benefits, barriers, and self-efficacy toward PA, PA-related affect, norms and support from family, peers, school, and providers, and PA options are recognized. In our day-to-day clinic, we observe that patients with JIA and their family are not always aware of the benefits of PA, anxiety toward a possible damaging effect of PA is not uncommon, and self-efficacy toward PA is often low. An initial period of active disease with pain and discomfort during PA makes it difficult to resume normal PA once the disease is inactive. It often takes time to cope. This is confirmed in our study.

We found a significant positive association between both AEE and PA level and time since diagnosis, which indicates that adolescents with JIA tend to display better PA behavior over time. Although we encourage patients to participate in PA classes in school, we often receive reports that children are forbidden to participate by PA teachers. Norms and social support are
often inadequate, which can be another possible explanation of low PA in adolescents with JIA. Is it safe for patients with JIA to participate in PA? Evidence is accumulating that it is safe, feasible, and acceptable for patients with JIA to participate in PA, exercise programs, and exercise testing\textsuperscript{33-36}. To increase their PA, it is unnecessary to increase vigorous PA, which can be difficult for adolescents with JIA. Westerterp demonstrated that subjects can increase their metabolic rate by exchanging low-intensity activities such as sitting in front of a screen for moderate-intensity activities such as walking or cycling\textsuperscript{37}.

In this study, we found a significant inverse association between both AEE and PA level and VAS well-being. Higher PA is associated with higher levels of well-being. Adolescents with JIA who have higher levels of PA feel better. This is in line with accumulating evidence that PA in youth is associated with better mental health, especially self-esteem and mood\textsuperscript{12,30,38}. We found no significant association between disease activity and PA, which implies that control over the disease does not automatically restore old PA levels, and disease management should therefore include strategies to restore normal PA.

We found a significant positive association between PA and absolute VO$_{2\text{peak}}$ in this study. In a previous study, we found lower aerobic fitness levels in adolescents with JIA compared with healthy age-matched peers\textsuperscript{10}. Low PA and fitness levels might possibly reinforce each other, leading to further deconditioning. Reduced work capacity can subsequently lead to limited career opportunities for adolescents with JIA. Between nonambulant subjects and elite endurance athletes, PA levels range from 1.2-4.5\textsuperscript{39}. In the general adult population, PA levels range from 1.2 for sedentary, inactive persons to 2.5 for very active persons\textsuperscript{37-40}. Adolescents with JIA had a mean PA level of 1.74 compared with 2.09 in the reference group. PA levels >2.5 can only be maintained by training and supplementing the diet with energy-dense, carbohydrate-rich formulas\textsuperscript{40}.

This study has a number of limitations. Various methods to measure PA are used and express PA in different terms. All of them have their limitations because PA is such a complex behavior. Therefore, it is difficult to compare the absolute PA between studies. We used a 3-day activity diary to get more insight into frequency, duration, and intensity of PA, but we are well aware that other aspects of PA (e.g., type of sport participation) can be important. The response rate in the JIA group is much higher than in the reference group because patients are more likely to comply with a study than students are to fill in a questionnaire. It is possible that there is a bias in the reference group toward those who are more active. To reduce this possible bias, we have emphasized the reason why we needed them to participate in a
reference group. We informed them about JIA and the consequences and motivated them by explaining that their participation could improve the care for patients with JIA.

In this study, the menstrual status of girls was not measured. Menstruation is associated with a number of physical, psychological, and behavioral changes. Kishali et al found that physical performance in 241 female athletes was not affected by the menstrual period, and pain decreased during training and competition. However, we do not know the effect of the menstrual cycle on PA in adolescent school-aged girls and therefore it is a possible confounding factor.

We conclude that adolescents with JIA have low PA levels compared with healthy controls, and are therefore at risk of losing the benefits of PA. Low PA is not related to disease activity; therefore, control over the disease does not restore previous PA levels. Interventions by pediatric rheumatologists are needed to increase PA levels in patients with JIA.

References

PA in adolescents with JIA
