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Generalized joint hypermobility and perceived harmfulness in healthy adolescents: impact on muscle strength, motor performance and physical activity level

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\textbf{ABSTRACT}

\textbf{Objective}: The first aim of this study was to determine whether adolescents with asymptomatic Generalized Joint Hypermobility (GJH) have a lower level of physical functioning (physical activity level, muscle strength and performance) compared to non-hypermobile controls. Secondly, to evaluate whether the negative impact of perceived harmfulness on physical functioning was more pronounced in adolescents with asymptomatic GJH.

\textbf{Methods}: Cross-sectional study. Sixty-two healthy adolescents (mean age 16.8, range 12–21) participated. Hypermobility (Beighton score), perceived harmfulness (PHODA-youth) and muscle strength (dynamometry), motor performance (Single-Leg-Hop-for-Distance) and physical activity level (PAL) (accelerometry) were measured. Hierarchical regression analyses were used to study differences in physical functioning and perceived harmfulness between asymptomatic GJH and non-hypermobile controls.

\textbf{Results}: Asymptomatic GJH was associated with increased knee extensor muscle strength (peak torque/body weight; PT/BW), controlled for age and gender (dominant leg; ß = 0.29; \( p = .02 \)). No other associations between asymptomatic GJH and muscle strength, motor performance and PAL were found. Perceived harmfulness was not more pronounced in adolescents with asymptomatic GJH.

\textbf{Conclusions}: Adolescents with asymptomatic GJH had increased knee extensor muscle strength compared to non-hypermobile controls. No other differences in the level of physical functioning was found and the negative impact of perceived harmfulness was not more pronounced in adolescents with asymptomatic GJH.

\textbf{Introduction}

Generalized joint hypermobility (GJH) is defined as an increased range of motion in most of the individual’s joints (Beighton, Grahame, and Bird, 2012). The prevalence of GJH in different child and adolescent populations varies from 2-55\%, depending on ethnicity, gender, age and the tests and criteria applied (Murray, 2006). For many individuals with GJH, flexible joints deliver a potential benefit in the performance of sporting activities such as dancing or gymnastics (Scheper et al., 2013a). However, for others, GJH can be disabling since it is related to symptoms such as chronic pain, joint instability, disturbed proprioception and soft tissue injuries, and is referred to as Generalized Hypermobility Spectrum Disorder (G-HSD) (Castori et al., 2017). G-HSD shows overlap with the hypermobile type of the Ehlers-Danlos Syndrome (hEDS) (Malfait et al., 2017). Both symptomatic conditions lack a specific genetic profile and it is referred to as G-HSD/hEDS.

In individuals with G-HSD/hEDS; a reduction in level of physical functioning (Fatoye et al., 2012; Voermans et al., 2010); decreased muscle strength (Engelbert et al., 2006; Fatoye et al., 2009); impaired proprioception (Fatoye et al., 2009; Sahin et al., 2008); reduced balance (Schubert-Hjalmansson, Ohman, Kyllerman, and Beckung, 2012) and decreased physical activity levels (PAL) (Rombaut et al., 2010) are commonly reported. Earlier studies also indicated that asymptomatic GJH alone was associated with decreased daily activities, such as walking distance and jumping capacity (Scheper et al., 2014b) and...
decreased muscle strength (Jindal, Narayan, Ganesan, and MacDermid, 2016; Scheper et al., 2014a). In addition, outcomes of a physical activity questionnaire showed that adolescents and young adults with asymptomatic GJH participated less during sports and outdoor activities and preferred more stable activities, such as walking and cycling compared to non-hypermobile controls (Scheper et al., 2014a). However, other studies could not confirm the reduced muscle strength (Jensen et al., 2013; Mebes et al., 2008) and altered physical activity level measured objectively with an accelerometer (Clinch et al., 2011) in adolescents and adults with asymptomatic GJH vs non-hypermobile controls. A possible explanation might be that the included population in the study of Jensen et al. (2013) and Mebes et al. (2008) was older than the included population in the studies that did find decreased muscle strength in asymptomatic GJH.

Thus, it remains unclear whether a lower level of physical functioning in G-HSD/hEDS is caused by GJH itself or whether it is due to pain or the anticipation of pain. It could be hypothesized that, due to GJH, an individual may learn to avoid or to be more careful during complex activities requiring more joint control, in order to prevent the development of musculoskeletal complaints or injuries. This behavior seems in line with avoidance behavior described in the fear-avoidance model to explain the disabling role of pain-related fear in chronic pain (Leeuw et al., 2007; Simons and Kaczynski, 2012). However, it is unclear whether individuals with asymptomatic GJH also perceive complex activities as potentially more harmful compared to individuals without GJH. Therefore the aim of this study was to determine whether adolescents with asymptomatic GJH have lower physical functioning levels, by assessing muscle strength, motor performance and PAL compared to non-hypermobile adolescents. In addition, the second aim was to evaluate whether the negative impact of perceived harmfulness on muscle strength, motor performance and PAL was more pronounced in adolescents with asymptomatic GJH compared to non-hypermobile adolescents.

**Methods**

**Participants**

In this cross-sectional study, sixty-two healthy adolescents (mean age 16.8, sd 2.3, range 12–21) were recruited in the Southern area of the Netherlands. The adolescents had good understanding of the Dutch language. Exclusion criteria were chronic musculoskeletal pain and specific medical conditions/disorders influencing physical functioning such as acute or recurrent musculoskeletal pain. The study protocol was approved by the Medical Ethics Committee of the Academic Maastricht University/University Hospital Maastricht, the Netherlands (METC number: 15-4-052).

**Procedure**

Adolescents were included in three different ways. First, adolescents were verbally informed about the purpose of the study on a local high school. Second, adolescents responded on a pamphlet that was presented at two institutes for higher education (Zuyd University of Applied Science and Maastricht University). Third, adolescents were asked from the personal network of the research group. Adolescents, that indicated to be interested in participation received an information letter and after a week, a researcher (TvM/NS/TH) contacted them by telephone or by mail to ask whether they were willing to participate in the study. All adolescents who participated provided written informed consent. Adolescents younger than 18 years needed written approval from their parents and/or caregivers.

After written approval all outcome measures were collected by a physical therapist during a 1 hour session. First, sociodemographic variables (age, gender, ethnicity of the father and mother, education level and if applicable having a (part time) job), pain intensity and the perceived harmfulness were collected. Further height and weight were measured in a standardized method without heavy clothing and shoes. BMI was calculated as weight in kilograms divided by the square of height in meters. Then, the physical functioning (i.e. isokinetic muscle strength and endurance and motor performance) was assessed and GJH was measured using the Beighton Score (BS). At last, adolescents were instructed about the use of the accelerometer, which measured PAL. The accelerometer had to be worn during 7 consecutive days.

**Measurements**

**Hypermobility**

The presence of hypermobility was assessed using the BS, with a standardized protocol (Smits-Engelsman, Klers, and Kirby, 2011). The BS consists of 9 functional tests (hyperextension of the knees, elbows and little fingers, thumb apposition to the forearm and trunk flexion) and scored dichotomously with a maximum score of 9 points. In a recently published consensus statement a cutoff point of 5 out of 9 for adults up to the age of 50 and a cutoff point of 6 out of 9 for pre-pubertal children and adolescents was recommended (Juul-Kristensen et al., 2017; Malfait et al., 2017). Based on these findings, the adolescents were assigned to one of two groups: a group with asymptomatic GJH (GJH; BS ≥ 6 for < 18 years; and BS ≥ 5 for ≥ 18 years)
or a group without asymptomatic GJH (non-GJH; BS < 6 for < 18 years and BS < 5 for ≥ 18 years). The BS is a valid instrument to evaluate GJH in elementary schoolchildren (Smits-Engelsman, Klerks, and Kirby, 2011).

**Pain intensity**
Pain intensity was measured with three 100-mm visual analogue scales (VAS): 1) current pain; 2) the worst/most severe pain experienced in the last week; and 3) the least pain experienced in the last week. The VAS pain is a reliable and valid measure for pain intensity in children older than 8 years (Stinson et al., 2006). The mean of these 3 VAS scores was calculated and used to express pain intensity in the analyses.

**Perceived harmfulness (PHODA-youth)**
The Photograph Series of Daily Activities for youth (PHODA-youth), which has been found to be valid and reliable in adolescents with chronic musculoskeletal pain (Verbunt et al., 2015), was used to measure perceived harmfulness. The PHODA-youth contains 51 age-specific activities and social situations and consists out of 3 categories: 1) activities of daily living and household (PHODA-ADL [13 items]); 2) intensive physical activities (PHODA-PA [27 items]); and 3) social activities (PHODA-SA [11 items]). Adolescents rate the photographs from 0 (“not harmful at all”) to 10 (“extremely harmful”), where higher scores indicated higher levels of perceived harmfulness.

**Physical functioning**
To represent the level of physical functioning; isokinetic muscle strength and endurance, motor performance and physical activity level were assessed.

**Muscle strength**
The Biodynamic System 3 Pro dynamometer* (Biodex Medical Systems, Shirley, NY, USA), which is a reliable and valid isokinetic dynamometer (Drouin et al., 2004), was used to test isokinetic knee extensor and flexor strength in both legs. The adolescent’s leg dominance was recorded by asking which leg was preferred for kicking a ball. The set-up of Rombaut et al. (2012) was used, where the adolescent was positioned in an upright sitting position and the tested leg was stabilized with a fixation strap. The lever arm was attached to the adolescent’s lower leg by a padded cuff 2 cm proximal to the medial malleolus, and the axis of movement of the dynamometer was in line with the axis of movement of the knee extension/flexion. After one practice repetition to become familiar with the movement and velocity, five repetitions of maximal voluntary concentric knee extension and flexion were performed at the angular velocity of 60°/second. Peak torque (PT; Nm) was assessed and is the highest muscular force output similar to one repetition maximum effort in isometric muscle work and represents the muscle’s maximum strength capability. PT/body weight is the PT normalized for body weight, used to standardize and compare scores and was used for further analyses.

**Muscle strength endurance**
The same setup as described above was used for measuring isokinetic muscle strength endurance in both legs. The adolescent had to perform 30 repetitions of maximal concentric knee extension and flexion with an angular velocity of 240°/second. The test was performed 60 seconds after the isokinetic test of 60°/second. Total work (J) is the work produced throughout the test and represents the muscle’s capability.

**Motor performance**
The Single-Leg-Hop-for-Distance (SLHD) is a dynamic motor performance test (Junge et al., 2015) measuring joint stability and coordination (Gustavsson et al., 2006), which might be decreased in asymptomatic GJH. The SLHD has shown high intra-subject reliability (Ross, Langford, and Whelan, 2002). The method of Junge et al. (2015) was used, where the adolescent stood on the test leg and then hopped as far as possible allowing arm swing assistance and landed on the same leg. The adolescent was instructed to control their landing and hold the landing foot in place until the distance was registered. After one practice hop, three valid hops with both legs were performed with a resting period of 30 seconds in between. The greatest distance measured in centimeters form the toe at the push off to the heel at the place the adolescents landed, for the dominant as well as the non-dominant leg was used for the analyses.

**Physical activity level**
The level of physical activity (PAL) was measured using a tri-axial accelerometer (AX3®; Axivity, Newcastle, UK). The accelerometer was attached to the hip at the dominant side of the body with the USB port at the downsize, medial to the spina iliaca anterior superior (SIAS), using plastic film (Tegaderm Film; 10 × 12 cm) and had to be removed during the performance of activities that could damage the monitor, such as contact sports and swimming. Bathing and showering was allowed with the accelerometer. Each adolescent received a diary to collect information on data interruption and was asked to register non-wearing time and the reason for doing this (Verbunt, Huijnen, and Seelen, 2012). Furthermore, wake up time, sleeping and school hours were noted. Nighttime and periods of non-wearing activities were excluded from the analysis. To be included as a valid
score, a minimum of three weekdays with at least 10 hours of recording and one weekend day with at least 8 hours of recording had to be available during the 7-day monitoring period (Ottevaere et al., 2011; Trost, McIver, and Pate, 2005). Data processing was performed using Matlab® (The Math Works Inc., Natick, USA). To obtain activity counts, an algorithm was designed based on the method, which was used for the Actiwatch 7® (Philips, Eindhoven, Netherlands). Using this algorithm, the acceleration signals were converted into one resultant acceleration signal. This signal was rectified and filtered using a high pass filter (HPF) at 3 Hz and a low pass filter (LPF) at 10 Hz. The highest recorded sample per second was selected in the filtered and rectified data and summed per minute. This counts/minute signal was used for all further calculations. Daily uptime was defined as the period between getting up and going to sleep and was presented in minutes.

PAL was expressed in three quantities: 1) Total activity during uptime, calculated as the total sum of counts during uptime (Huijnen et al., 2010). Data imputation was used to compensate for non-wearing time during contact sports. Values during non-wearing time were replaced by 2 times the mean score per minute of the previous day (Huijnen et al., 2010); 2) Mean activity level during 24 hours, expressed as the mean number of counts per minute per day. In this second method, sleeping time is included in the total score; and 3) Peak activity level, determined as the highest number of counts achieved in a single minute per daytime wake period (Wilson and Palermo, 2012). In addition, total activity during uptime and peak activity level were calculated separately for the weekend days, weekdays, school hours, and non-school hours.

### Statistical analysis

Data analysis was performed using IBM Statistics for Windows®, v23.0. (IBM Corp, Armonk, NY, USA). Normality of the variables was checked by eye balling using histograms and the Kolmogorov-Smirnov goodness-of-fit-test. Descriptive data of the anthropometrics and sociodemographic measures, perceived harmfulness, and pain intensity of the GJH group and the non-GJH group are presented as mean ± standard deviation (SD) in the case of normality of the variable. In the case of a non-normal distribution the median and interquartile range (IQR) are presented. Group differences between non-GJH and GJH were tested using an independent sample t-test, Mann-Whitney test or Kruskal-Wallis test for numerical variables and a Chi-square test for categorical variables.

Hierarchical regression analyses were used to study the hypothesis that adolescents with asymptomatic GJH have a decreased level of physical functioning (represented by muscle strength, muscle strength endurance, motor performance and PAL) compared to non-hypermobile adolescents and in addition, whether the negative impact of perceived harmfulness is more pronounced in adolescents with asymptomatic GJH. Analyses were performed per representative of physical functioning in three steps: 1) representative of physical functioning (i.e. muscle strength) was introduced as the dependent variable and age, gender (male = 1; female = 0) and hypermobility (GJH = 1; non-GJH = 0) were introduced as independent variables; 2) PHODA-youth was added; and 3) interaction term (PHODA-youth*GJH/non-GJH) was introduced. In case of a significant interaction, additional regression analyses were performed for both groups separately. This procedure was repeated with the other representative of physical functioning (i.e. muscle strength endurance, motor performance and PAL [total activity during uptime]) as independent variables. For all independent variables, the association with the outcome was presented by the standardized regression coefficient ($\beta$) and $p$-value. As muscle strength endurance (extension dominant leg and extension non-dominant leg), the PHODA-youth and age did not meet the assumption of normality, these variables were log transformed prior to analysis. After transformation, skewness and kurtosis values of the scales were in the acceptable range of −1 and +1. For all regression analysis, a collinearity check was performed. Collinearity was considered a problem when the variance inflation factor (VIF) was above 10 (Myers, 1990). To compare the different PAL conditions between the GJH and non-GJH group, independent t-tests or Mann-Whitney tests were used. P-values less than 0.05 were considered statistically significant.

### Results

#### Descriptive analysis

Sixty-two adolescents (47 females/15 males) participated in the study. Table 1 presents the characteristics per group (GJH/non-GJH). Eleven adolescents (18%) fulfilled the criteria for asymptomatic GJH, only 1 male had GJH. There was a significantly higher Beighton ($p = 0.01$) and higher age ($p = 0.02$) in the GJH group compared to the non-GJH group. In addition, significantly more adolescents in the GJH group participated in tertiary education (vocational education or university of applied sciences or university) compared to the non-GJH group ($p = 0.04$). No other significant differences between the GJH and the non-GJH group with respect to gender, weight, height, BMI, ethnicity, part time job and pain intensity were found.
Table 1. Characteristics of the study sample of adolescents with or without asymptomatic GJH.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>GJH (n = 11)</th>
<th>Non-GJH (n = 51)</th>
<th>Test statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females/males, n</td>
<td>10/1</td>
<td>37/14</td>
<td>p = .27</td>
</tr>
<tr>
<td>Beighton, n *</td>
<td>6.0 (5.0–7.0)</td>
<td>2.0 (2.0–3.0)</td>
<td>U = 8, z = −5.23, p ≤ .00</td>
</tr>
<tr>
<td>Age, y *</td>
<td>18.0 (16.0–20.0)</td>
<td>16.0 (15.0–18.0)</td>
<td>U = 158, z = −2.28, p = .02</td>
</tr>
<tr>
<td>Weight, kg a</td>
<td>63.1 (52.0–73.7)</td>
<td>59.0 (53.1–69.7)</td>
<td>U = 259, z = −0.40, p = .69</td>
</tr>
<tr>
<td>Height, cm b</td>
<td>169.7 ± 10.1</td>
<td>170.0 ± 9.0</td>
<td>%90 = 0.09 (0.28,3.06)</td>
</tr>
<tr>
<td>BMI, kg/m² a</td>
<td>22.4 (18.5–22.4)</td>
<td>21.5 (18.9–23.0)</td>
<td>U = 259, z = −0.40, p = .69</td>
</tr>
<tr>
<td>Ethnicity father, n (%)</td>
<td></td>
<td></td>
<td>H1 = 0.01, p = .92</td>
</tr>
<tr>
<td>–Caucasian</td>
<td>10 (90.9)</td>
<td>48 (94.2)</td>
<td>H1 = 0.00, p = .97</td>
</tr>
<tr>
<td>–Arabic</td>
<td>1 (9.1)</td>
<td>2 (3.9)</td>
<td>H1 = 4.09, p = .04</td>
</tr>
<tr>
<td>–Latin American</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
<td>p = .48</td>
</tr>
<tr>
<td>Ethnicity mother, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–Caucasian</td>
<td>10 (90.9)</td>
<td>48 (94.2)</td>
<td></td>
</tr>
<tr>
<td>–Arabic</td>
<td>1 (9.1)</td>
<td>2 (3.9)</td>
<td></td>
</tr>
<tr>
<td>–Latin American</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Education level, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–Primary education</td>
<td>0 (0.0)</td>
<td>1 (2.0)</td>
<td></td>
</tr>
<tr>
<td>–Secondary education</td>
<td>3 (27.3)</td>
<td>30 (58.8)</td>
<td></td>
</tr>
<tr>
<td>–Tertiary education</td>
<td>8 (72.7)</td>
<td>20 (39.2)</td>
<td></td>
</tr>
<tr>
<td>Part time job (yes/no), n</td>
<td>9/2</td>
<td>33/18</td>
<td></td>
</tr>
<tr>
<td>Pain intensity a</td>
<td>0.5 (0.0–0.9)</td>
<td>0.3 (0.0–1.1)</td>
<td>U = 276, z = −0.09, p = .93</td>
</tr>
</tbody>
</table>

Abbreviations; GJH: group with asymptomatic hypermobility; Non-GJH: group without asymptomatic hypermobility; BMI: body mass index.

Table 2 presents the results of the level of perceived harmfulness on the PHODA-youth and all subscales. Results showed that the level of the perceived harmfulness was very low on all subscales related to the total score range. There were no significant differences regarding the level of perceived harmfulness between the GJH group and the non-GJH group (Table 2).

Muscle strength

Table 3 presents the results of muscle strength. The first step showed that having GJH (β = 0.29; p = .02) and a higher age (β = 0.26; p = .04) were both associated with increased knee extensor muscle strength (PT/BW). The mean difference of the knee extensor muscle strength for respectively females and males in the GJH group was 45% and 46% higher in the dominant leg and 36% and 28% higher in the non-dominant leg compared to the females and males in the non-GJH group. In the second step, the PHODA-youth was introduced. No significant association between the PHODA-youth score and muscle strength (PT/BW) were found. After adding the interaction term (PHODA-youth*GJH/non-GJH) in step 3, no significant association was found. There were no significant associations regarding the knee flexion muscle strength (PT/BW). The analyses with the non-dominant leg were not presented but results were comparable to the findings as presented of the dominant leg.

Muscle strength endurance

For the flexor and extensor muscle strength endurance (total work), there were no differences between the GJH group and the non-GJH group (Table 3). Only a higher age was associated with a higher knee extensor (β = 0.27; p = .04) and flexor (β = 0.32; p = .02) muscle strength endurance (total work). Analyses with the non-dominant leg were not presented but results were comparable to outcomes of the dominant leg as presented.

Motor performance

According to motor performance (SLHD), there were no significant differences between the GJH group and the non-GJH group (Table 3). Results in the first step showed that male adolescents had a significantly higher score on the SLHD (β = 0.45, p < .01). In the second
step, the PHODA-youth was associated with motor performance ($\beta = -0.33, p = .01$), indicating that higher perceived harmfulness was associated with a lower score on the SLHD, but this finding was not different for those with and without hypermobility. The analysis with the non-dominant leg was not presented but again results were comparable with the results of the dominant leg.

**PAL**

The accelerometer data of 49 adolescents (GJH, $n = 8$; non-GJH, $n = 41$) were used for analysis of PAL. Data of thirteen of the 62 adolescents were excluded from the analysis due to invalid scores caused by dysfunction of the AX3 ($n = 3$) or due to not fulfilling the pre-determined criteria of the weekly registration for a valid accelerometer registration-period ($n = 10$). During PAL measurements, 15 adolescents had no school obligations due to holidays. Therefore only 34 (GJH, $n = 5$; non-GJH, $n = 29$) participated in school. Figure 1 presents the overall total activity during uptime and total activity during uptime per week and weekend day and school and non-school hours for the GJH and non-GJH group separately. There were no significant differences between the GJH and the non-GJH group for all PAL conditions. In addition, daily uptime was not significantly different between both groups.

In Table 3 the outcome of the regression model with PAL (total activity during uptime) showed that in the first step a younger age was associated with an increased

<table>
<thead>
<tr>
<th>Model Steps</th>
<th>Muscle Strength</th>
<th>Muscle Strength endurance</th>
<th>Motor Performance</th>
<th>Physical Activity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Extension</td>
<td>Flexion</td>
<td>Extension</td>
<td>Flexion</td>
</tr>
<tr>
<td></td>
<td>$\beta$</td>
<td>$p$</td>
<td>$\beta$</td>
<td>$p$</td>
</tr>
<tr>
<td>Step 1</td>
<td>0.29</td>
<td>0.02</td>
<td>0.18</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0.26</td>
<td>0.04</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Gender</td>
<td>0.03</td>
<td>0.79</td>
<td>0.10</td>
</tr>
<tr>
<td>Step 2</td>
<td>PHODA-youth</td>
<td>-0.11</td>
<td>0.41</td>
<td>-0.15</td>
</tr>
<tr>
<td>Step 3</td>
<td>PHODA-youth *GJH/non-GJH</td>
<td>-0.12</td>
<td>0.60</td>
<td>-0.06</td>
</tr>
<tr>
<td>Result of the regression analysis</td>
<td>$R^2$</td>
<td>0.20</td>
<td>0.07</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Abbreviations; PHODA: Photographs Series of Daily Activities; GJH: group with hypermobility; non-GJH: group without hypermobility. Muscle strength, muscle strength endurance and motor performance are only presented for the dominant leg. Values presented are the standardized regression coefficient ($\beta$). $P$-values from the separate variables are from the t-tests in the equation.
level of PAL ($\beta = -0.39; p < .01$). There were no significant differences in PAL between the GJH group and the non-GJH group. The analyses with mean activity level during 24 hours and peak activity level instead of total activity during uptime were not presented but confirmed the findings of total activity during uptime.

**Discussion**

This study indicates that adolescents with asymptomatic GJH have no lower physical functioning levels, regarding muscle strength, motor performance and PAL compared to non-hypermobile adolescents. Contrary to expectations, adolescents with asymptomatic GJH have increased muscle strength of the knee extensors of the dominant and non-dominant leg compared to non-hypermobile adolescents. In addition, the negative impact of perceived harmfulness was not more pronounced in adolescents with asymptomatic GJH.

In contradiction to earlier studies that did find a lower level of physical functioning in adolescents and young adults with asymptomatic GJH compared to non-hypermobile controls (Jindal, Narayan, Ganesan, and MacDermid, 2016; Scheper et al., 2014a, 2014b) our results showed that adolescents with asymptomatic GJH have no decreased muscle strength, motor performance and PAL compared to non-hypermobile adolescents. However, the findings of the current study were consistent with results of earlier studies in adolescents and adults with asymptomatic GJH compared to non-hypermobile controls (Clinch et al., 2011; Jensen et al., 2013; Junge et al., 2015; Mebes et al., 2008). In addition, a recent study also showed that no differences in physical functioning, measured as lower extremity function and motor performance, occurred between adolescent athletes with asymptomatic GJH and non-hypermobile adolescent athletes (Schmidt et al., 2017). A possible explanation between the different outcomes of PAL could be that the current study and Clinch et al. (2011) used accelerometry as objective measurement, whereas Scheper et al. (2014a) used a subjective measure. So, adolescents with GJH might perceive an altered PAL but objective measurements did not confirm these beliefs. Furthermore, our study, Jensen et al. (2013), Junge et al. (2015), and Mebes et al. (2008) found no differences in muscle strength of the lower extremity in contrast to Jindal, Narayan, Ganesan, and MacDermid (2016) and Scheper et al. (2014a) who also measured upper extremity. Therefore, it might be recommendable to measure lower and upper extremity muscle strength in future studies as well as subjective and objective measurements of PAL. The results of the current study even showed that muscle strength of the knee extensors was increased in adolescents with asymptomatic GJH compared to non-hypermobile adolescents, which was also found in a study of Mebes et al. (2008) with a female population (aged 27.2–28.1 years). Thus, having asymptomatic GJH appeared to be non-related to a decrease in physical functioning. However, more research according to the updated cutoff values of the recent published consensus statement (Juul-Kristensen et al., 2017; Malfait et al., 2017) is needed to confirm these findings and whether muscle strength is even increased in adolescents with asymptomatic GJH.

The objective physical measurements in the current study showed that, having asymptomatic GJH was not associated with decreased physical functioning. In patients with G-HSD/hEDS: decreased muscle strength (Engelbert et al., 2006; Fatoye et al., 2009); reduced balance (Schubert-Hjalmarsson, Ohman, Kyllerman, and Beckung, 2012); decreased PAL; and lower sport participation (Rombaut et al., 2010; Schubert-Hjalmarsson, Ohman, Kyllerman, and Beckung, 2012) were found compared to pain-free non-hypermobile controls. These results seemed to imply that a lower level of physical functioning in patients with G-HSD/hEDS could not be explained by GJH alone. This is also confirmed in a recent longitudinal study in children with G-HSD/hEDS, in which multi-systemic dysfunction (e.g. skin, cardiovascular, and gastrointestinal involvement), high levels of pain and fatigue and loss of postural control were found to be the most important constructs for functional impairment in terms of performance and capacity (Scheper et al., 2017). However, given that the findings of the current study are based on a small number of adolescents with asymptomatic GJH, this interpretation should be treated with caution.

Results of the current study also showed that perceived harmfulness was not associated with a decreased muscle strength nor PAL. However, perceived harmfulness was associated with a lower score on the motor performance task. Although hypothesized, this finding was not more pronounced in adolescents with asymptomatic GJH. One recent study in adolescents with chronic musculoskeletal pain found that pain-related fear was associated with a higher level of disability whereas G-HSD/hEDS was not associated with a higher level of disability (van Meulenbroek, Huijnen, Wiertz, and Verbunt, 2017). Whether pain, anticipation of pain and pain-related fear might indeed contribute more to impaired physical functioning levels in G-HSD/hEDS, as has been found in other chronic pain-conditions (Cohen, Vowles, and Eccleston, 2010; Martin, McGrath, Brown, and Katz, 2007), should be further explored.

**Limitations**

This study has some limitations. The first limitation is a relatively large number of analyses performed in the
current study. Therefore, there is an increased risk of a Type I error. As mentioned earlier, a second limitation is the small group of adolescents with asymptomatic GJH. However, the prevalence of hypermobility in this study is 18% which is comparable with other studies performed in a general population, despite the different cutoff points (Remvig, Jensen, and Ward, 2007; Scheper et al., 2013b). Further research should be conducted in a larger population. A third limitation is the absence of continuous physical activity registration due to contact sports or swimming. This might result in an underestimation of the participant’s actual activity level. Also the lower number of PAL measurements during school and exclusion of 10 adolescents due to not fulfilling the predetermined criteria for a valid measurement might affect the results. A fourth limitation of this study is the use of the PHODA-youth. The scores on the PHODA-youth and all subscales were low compared to the range. Therefore, it questions the validity of the assessment of perceived harmfulness in a pain-free situation. The PHODA-youth has not been validated in healthy pain-free adolescents yet. Further research is needed to evaluate the assumption that perceived harmfulness can indeed be measured with the PHODA-youth in a pain-free population. The finding that in adults, fear of injury/perceived harmfulness, as assessed by the Tampa Scale for Kinesiophobia, can be used in a pain-free population may support the assumption (Houben et al., 2005). The final limitation is the cross-sectional design of the study, which meant no causal relationships could be confirmed. Future studies should employ longitudinal designs to examine associations over time. Evidence has shown that GJH is a risk factor for developing chronic musculoskeletal pain (Sohrbeck-Nohr et al., 2014; Tobias et al., 2013) and therefore differences in physical functioning levels before the onset of chronic musculoskeletal pain may help to unravel the influence of GJH on physical functioning levels in adolescents who will or will not develop chronic musculoskeletal pain.

Clinical implications
This study has clinical implications. A lower level of physical functioning in adolescents with G-HSD/hEDS is not solely caused by GJH. It is therefore important that, in clinical practice, treatment of adolescents with G-HSD/hEDS should also focus on other contributing factors such as pain, fatigue, multi-systemic dysfunction, loss of postural control and pain-related fear (Leeuw et al., 2007; Scheper et al., 2017; Vlaeyen and Linton, 2000).

Conclusion
Adolescents with asymptomatic GJH had no lower level of physical functioning (normal muscle strength, motor performance and PAL) compared to non-hypermobile controls. Contrary to expectations, knee extensor muscle strength was even significantly increased in adolescents with asymptomatic GJH. The negative impact of perceived harmfulness was not more pronounced in adolescents with asymptomatic GJH.

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Declaration of Interest
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