Hypermobility and Musculoskeletal Pain in Adolescents

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Objective To determine the prevalence of generalized joint hypermobility (GJH) in a large cohort of Australian children and determine the associations between GJH and musculoskeletal pain.

Study design This is a cross-sectional analysis of the Western Australian Pregnancy Cohort (Raine) Study. Hypermobility was measured in 1584 participants at 14 years of age using the Beighton scoring system, along with a range of other factors including musculoskeletal pain status. Logistic regression models were used to assess independent associations of GJH with factors of interest.

Results The prevalence of GJH was 60.6% and 36.7% in girls and boys, respectively, when defined as a Beighton score of ≥4; when defined as ≥6, it was 26.1% and 11.5%. In girls, positive associations between GJH and higher socioeconomic status and better motor competence were observed. In boys, positive associations between GJH and lower body mass index were observed. After adjusting for potential confounders, an association between number of pain areas in the last month and made worse with sport were identified in boys but not girls.

Conclusion The high prevalence rates of GJH as defined by commonly used Beighton cutoff values in this cohort highlight the need to question the appropriateness of these cutoffs in future studies. Future prospective studies of the association between GJH and musculoskeletal pain should be adjusted for confounding variables identified in this study, and be powered for sex-specific analyses owing to the differing prevalence rates and hypermobility correlates in male and female samples. *(J Pediatr 2017;181:213-21).*

Generalized joint hypermobility (GJH) is defined as greater than normal joint laxity across multiple joints, and is a diagnostic criterion for a range of heritable connective tissue disorders.[1] Joint hypermobility syndrome (JHS), which is diagnosed clinically and indistinguishable from Ehlers-Danlos syndrome (hypermobility type), is considered to be the symptomatic end of the GJH spectrum, with arthralgia for >3 months being a major diagnostic, although not necessarily defining, criterion according to the revised Brighton criteria.[2,3] However, because GJH also occurs in the absence of joint pain, and there is a lack of consensus on the criteria for JHS,[1] the association between GJH and pain at a population level is of interest.

Epidemiologic studies of GJH commonly use the Beighton scoring system,[4,5] a series of 9 dichotomous joint extensibility tests that demonstrates moderate to high intertester repeatability.[6] A Beighton score of ≥4 has been used commonly to indicate GJH in adults[2,3]; however, a higher threshold has been advocated for use in children owing to the greater prevalence of joint laxity.[1,6-10]

When considering children of mixed ages (3-18 years), the prevalence of GJH has been reported at around 35% using a cutoff score of ≥4.[9,11-13] Although the cutoff for GJH differs between studies, in general higher prevalence rates have been attributed to female sex,[2,8,11] younger age,[4,10,11,14-17] non-Caucasian race,[2] malnutrition,[16] and sports that train flexibility such as dancing.[18]

The association between GJH and musculoskeletal pain (MSP) is contentious. Small-scale studies of clinical populations of children with JHS report that they experience greater pain intensity than comparison groups of children without JHS,[19,20] and that children with chronic MSP have been reported to have more hypermobile joints than pain free children in a small (n = 30) cross-sectional clinical study.[21] In contrast, the relationship between GJH and MSP is equivocal for children from the general population. A systematic review and meta-analysis of 15 cross-sectional studies reported no association between GJH and MSP in studies of Caucasian populations, but a potential association in Afro-Asian populations.[22] Additionally, studies reviewed did not adjust for any potentially confounding beyond age and sex.[22] Although longitudinal studies have provided some support for an association between GJH and MSP, the evidence for hypermobility as a causative factor for MSP is limited.[23-25]

BMI	Body mass index
GJH	Generalized joint hypermobility
JHS	Joint hypermobility syndrome
MAND	McCarron Assessment of Neuromuscular Development
MSP	Musculoskeletal pain

The first aim of this study is to define the prevalence and descriptive epidemiology of GJH in an Australian population. The second aim is to explore the association between GJH and self-reported MSP characterized by its presence in the last month, lasting >3 months, and made worse by sport.

Methods

This study was conducted using data from the Western Australian Pregnancy Cohort (Raine) Study (http://rainestudy.org.au/). This began as a pregnancy cohort of 2900 women attending antenatal clinics at King Edward Memorial Hospital in Perth, Australia, between 1989 and 1991, and resulted in 2868 children forming the cohort. This is a cross-sectional analysis of 1584 of the 1608 adolescents attending the 14-year follow-up, for whom both GJH and musculoskeletal data were available (**Figure**; available at www.jpeds.com). Comparative analysis at 14 years to census data showed that the cohort remained representative of the Western Australian population. Informed consent was obtained from participants and the study approved by the Ethics and Scientific Review Committee of Princess Margaret Hospital for Children and the Human Research Ethics Committee of Curtin University. Around the time of their 14th birthday, participants presented for a follow-up visit at the study assessment center, where they completed a computer-based questionnaire covering a broad range of factors, including pain status, and then a physical assessment that included measures of GJH and motor performance.

Generalized Joint Hypermobility

Joint hypermobility was measured using the Beighton scoring system.[4] The Beighton is a well-recognized and widely used scale of GJH with demonstrated validity and reliability[5,9,26] (**Appendix**; available at www.jpeds.com). Joint angles were determined using visual estimation without a goniometer. Joint hypermobility was defined using 2 criteria: (1) ≥4 hypermobile joints and (2) ≥6 hypermobile joints.[7] The application of the Beighton score in this study retained the original description of hyperextension of the metacarpophalangeal joint of the fifth finger[27] because pilot testing suggested this was the most reproducible method (**Appendix**). For the toe touching maneuver, this study applied the "most of their palms on the floor" rather than "palms rest easily on the floor[26] (**Appendix**).

Other Measures

For aim 1, similar constructs for comparison between adolescents with and without GJH were chosen as previously examined in the large 14-year-old cohort from the United Kingdom.[7] During the physical examination, height (m) was measured with a stadiometer with shoes removed and body weight (kg) with digital scales. The body mass index (BMI) was calculated from these measures. Children were classified as normal weight, overweight, or obese using recommended age- and sex-specific cutoffs for children.[28] Motor performance was evaluated using the McCarron Assessment of Neuromuscular Development (MAND).[29] The test consists of 10 items that are converted to the Neuromuscular Index with a mean of 100 and a standard deviation of 15.[29] Handedness for writing was part of the MAND assessment.[29] The MAND has criterion, content, and construct validity as well as adequate precision and responsiveness to motor impairment.[29,30]

As a measure of moderate to vigorous physical activity, participants were asked a question regarding the frequency of exercise causing them to be out of breath or to sweat outside of school hours,[31] with responses categorized as none, about 30 minutes a week, about 1 hour a week, about 2-3 hours a week, about 4-6 hours a week, and ≥7 hours a week. This question has demonstrated acceptable reliability and validity.[32,33] The ethnicity of each parent was ascertained at enrollment in the study by questionnaire and for the purposes of this analysis participants were deemed of Caucasian ethnicity if ≥1 parent endorsed it. Socioeconomic status was measured using the Socio-Economic Indexes for Area index of relative socioeconomic advantage and disadvantage[34] at the census district level using current residential address. This index is standardized against the Australian population with a mean of 1000 with a standard deviation of 100, and for interpretation of ORs was divided by 100 so that a unit change represents approximately 1 standard deviation. Pubertal status was determined by self-rated Tanner stages of pubertal development,[35] which has demonstrated sufficient validity for use in large epidemiologic studies.[36] Boys reported on 4-stage diagrams of pubic hair and girls on pubic hair and breast development. For a short period during the follow-up, 334 individuals (170 girls and 164 boys) were shown Tanner stage diagrams where there was ambiguity in the labelling, and data were treated as missing for this variable in these cases.

Musculoskeletal Pain

Participants were asked the following questions with reference to the arm or leg; neck/shoulder; and back: (1) Have you ever had (area) pain?; (2) Has your (area) been painful in the last month?; (3) Did your (area) pain last for >3 months?; and (4) Did playing sports make your (area) pain worse?

For the current study, 3 derived variables were constructed, indicating the number of areas the participant: (i) reported having pain in the last month, (ii) reported having pain for >3 months, and (iii) reported pain being made worse with sport, with possible values being 0 (none), 1 (1) or 2 (≥2). The questions were based on the Nordic Pain Questionnaire and have established validity and reliability for pain assessment[37-39] and are reported to be valid when compared with physical examination/interview in 10- to 16-year-old subjects.[40]

Statistical Analyses

Percentages were calculated for point prevalence estimates of GJH for both Beighton cutoff of ≥4 joints and ≥6 joints and for hypermobility at each test site, both combined and separately for boys and girls.

For aim 1, χ^2 analysis or independent t tests were used to assess group differences in variables of interest between those individuals with/without generalized hypermobility (as defined by Beighton cutoff of ≥4 joints and ≥6 joints), in boys and girls separately. Unadjusted ORs (with 95% CIs) for the presence