

# Sex of Preceding Sibling and Anthropometrics of Subsequent Offspring at Birth and in Young Adulthood: A Population-Based Study in Sweden

Aline Jelenkovic,<sup>1,2,3\*</sup> Karri Silventoinen,<sup>3,4</sup> Per Tynelius,<sup>5</sup> Samuli Helle,<sup>6</sup> and Finn Rasmussen<sup>5</sup>

<sup>1</sup>Department of Genetics, Physical Anthropology and Animal Physiology, University of the Basque Country UPV/EHU, Leioa, Spain

<sup>2</sup>IKERBASQUE, Basque Foundation for Science, Bilbao, Spain

<sup>3</sup>Department of Public Health, Hjelt Institute, University of Helsinki, Helsinki, Finland

<sup>4</sup>Population Research Unit, Department of Social Research, University of Helsinki, Helsinki, Finland

<sup>5</sup>Child and Adolescent Public Health Epidemiology, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

<sup>6</sup>Section of Ecology, Department of Biology, University of Turku, Turku, Finland

**KEY WORDS** body size; cost of reproduction; H–Y antigen; linear regression model; muscle strength

**ABSTRACT** In many mammal species with sexual dimorphism producing sons is energetically more demanding to the mother than producing daughters. Although some studies in humans have suggested that offspring born after a brother have a smaller birth weight and adult height when compared with those born after a sister, little is known about this intergenerational cost of producing sons. We aimed to study whether the sex of preceding sibling is associated with anthropometrics of the subsequent child at birth and in young adulthood. This population-based study was carried out on two data sets derived from the Swedish registers. Information on birth weight and length was obtained for 752,723 children of both sexes. Adult weight, height and muscle strength were available for 506,326 men. Multiple linear regression analyses showed that boys and girls born after a brother were,

respectively, 18 and 9 g lighter and 0.08 and 0.03 cm ( $P < 0.001$ ) shorter at birth than those born after a sister. Adjustment for gestational age decreased the magnitude of the associations [10 g and 0.04 cm ( $P < 0.001$ ) in men and nonsignificant estimates in women], suggesting that part of the lower mean birth weight and length of individuals born after a brother was due to a shorter gestation. In young adulthood, men with a preceding brother showed 0.16 kg more in weight, 0.3% higher body mass index ( $P < 0.001$ ) and a trend towards reduced height and muscle strength. Our results suggest that even though the sex of the previous child is associated with the anthropometrics of the subsequent child, the effect sizes are very small questioning whether this mechanism has adaptive value in contemporary humans. *Am J Phys Anthropol* 154:471–478, 2014. © 2014 Wiley Periodicals, Inc.

The theory of life history evolution states that reproduction is energetically costly upon parents (Roff, 2002). Reproductive costs can compromise an individual's ability to survive and invest in new offspring, and thus tradeoffs between current and future reproductive investments are expected (Roff, 2002). In several sexually dimorphic mammal species where males are larger than females there is evidence that producing sons is energetically more demanding to the mother than producing daughters (e.g., Bérubé et al., 1996). In humans, sons have a faster intrauterine growth rate (Marsal et al., 1996) and heavier weight and size at birth (Hindmarsh et al., 2002; Loos et al., 2001), as well as higher energy requirements during gestation (Tamimi et al., 2003) and lactation (Butte et al., 2000; da Costa et al., 2010; Sellen, 2007). Giving birth to and raising sons versus daughters has also been associated with adverse long-term consequences such as reduced maternal life span in preindustrial populations (e.g., Helle et al., 2002; Helle and Lummaa, 2013); however, little is known about the consequences of producing sons for mothers' ability to invest in future offspring in humans.

In line with the life-history theory, some studies have suggested that birth weight is lower in those children

born after a son than in those born after a daughter (Blanchard and Ellis, 2001; Cote et al., 2003; Magnus et al., 1985; Nielsen et al., 2008; Rickard, 2008; Trotnow et al., 1976), but whether this association exists in children of both sexes or only in boys remains unclear. In a Danish study, having one or two brothers respectively was associated with a reduced birth weight of 29 g and 38 g on later born boys and of 17 and 21 g on later born

Grant sponsor: The Basque Government's Department of Education, Universities and Research (DEUI); Grant sponsor: The Academy of Finland (#266592); Grant sponsor: The Turku Collegium for Science and Medicine.

\*Correspondence to: Aline Jelenkovic; Department of Public Health, Hjelt Institute, University of Helsinki, Helsinki 00014, Finland. E-mail: aline.jelenkovic@helsinki.fi

Received 10 September 2013; accepted 30 April 2014

DOI: 10.1002/ajpa.22534

Published online 13 May 2014 in Wiley Online Library (wileyonlinelibrary.com).

girls, compared with later born siblings with no brothers (Nielsen et al., 2008). This study additionally detected that part of this association was explained by a shorter gestational age among later born siblings with brothers (Nielsen et al., 2008). The only study that analyzed the relationship between the sex of preceding siblings and birth length of a later born child found nonsignificant differences between the mean birth length of boys with older sisters (51.68 cm) and that for boys with older brothers (51.40 cm) (Cote et al., 2003). These findings thus suggest that the maternal reproductive costs could also depend on the sex or sex ratio of previously born offspring. Alternatively, some authors have suggested that this pattern of relationships may reflect a maternal immune response against male-specific minor histocompatibility (H–Y) antigens (e.g., Blanchard and Ellis, 2001; Nielsen et al., 2008).

According to the “developmental origins of adult disease” (DoHAD) hypothesis, environmental conditions experienced early in the life cycle can profoundly influence an organism’s biology and long-term health (Barker, 1998). This hypothesis, for which animal studies have shown a strong epigenetic basis (Gluckman and Hanson, 2006), is supported by epidemiological studies in humans linking low birth weight to increased risk for the development of several diseases in adulthood such as cardiovascular diseases (CVD) (Lawlor et al., 2005; Risnes et al., 2011). Well-known risk factors for CVD are obesity, reduced stature and weak muscle strength (Melanson et al., 2001; Silventoinen et al., 2009). Both weight and length at birth have shown to be predictors of adult weight and height (Eide et al., 2005). Birth weight has also been positively associated with later body mass index (BMI) (Rasmussen and Johansson, 1998) and obesity (Parsons et al., 1999), but the evidence is still mixed (Brisbois et al., 2012; Rogers and EURO-BLCS Study Group, 2003). The relationship is also positive with lean body mass (LBM) and muscle strength (Dodds et al., 2012; Rogers and EURO-BLCS Study Group, 2003) but negative with relative adiposity, thus suggesting that the association between birth weight and BMI does not necessarily reflect increased adiposity at higher birth weight (Rogers and EURO-BLCS Study Group, 2003). These anthropometric phenotypes are in turn related to reproductive performance. Models of male life history assume that men invest in traits such as stature, lean mass and strength, which despite metabolically costly, benefit reproductive fitness indirectly by boosting qualities like competitive ability and attractiveness (Ellison, 2003; Kuzawa, 2007). Therefore, the long-term associations between birth weight and sexually dimorphic traits in adulthood suggest that the early environment may also have long-term consequences for male reproductive fitness. In fact, birth weight itself has been positively related to the probability of marriage in men (Phillips et al., 2001; Vagero and Modin, 2002), but not in women (Vagero and Modin, 2002).

Since individuals born after a brother seem to be lighter at birth and reduced birth weight is associated with an increased risk for the development of several diseases in adulthood, we should expect that there may be long-term consequences of producing sons, not only for the mother but also for her subsequent offspring. In fact, being born after a brother has been related to decreased lifetime reproductive success in preindustrial Finland (Rickard et al., 2007). To the best of our knowledge, the only attempt to shed light on the association

between the sex of the preceding sibling and anthropometrics in adulthood was a study carried out in merely 79 men and women aged 18–55 years of the University of Glasgow (Rickard, 2008). The study reported that individuals born after a brother were 2.4% shorter and 7% lighter than those born after a sister; however, additional control for adult height suggested that older sibling sex-mediated differences in weight were explained by older sibling sex-mediated differences in height (Rickard, 2008). Thus, the association between the sex of the previous sibling and the adult body size of the subsequent offspring needs to be more extensively analyzed using larger and more representative samples.

Accordingly, the aim of this study was twofold. First, to test whether children born to mothers who had a son in the previous reproductive event have a lower birth weight and length than those born after a sister, and whether this effect depends on the sex of the later-born sibling. Second, to explore whether the sex of the preceding sibling is associated with height, weight, BMI and muscle strength of young adult men in the general Swedish population. The direction and magnitude of these relationships are important to elucidate the underlying biological mechanisms.

## MATERIALS AND METHODS

### Study sample

This study was based on a record-linkage between the Swedish Multi-Generation Register (MGR), the Medical Birth Register (MBR), the Military Service Conscription Register (MSCR) and the Swedish Population and Housing Censuses (PHCs) using personal identification numbers. All men and women in Sweden born 1951–1987 were identified in the MGR and comprise the study population from which two data sets were derived: the birth data set (BirthData) and the adult data set (AdultData). Identifiers for the biological mother, maternal age, birth year, birth order, and sex were obtained from the MGR. Families with multiple births were removed from the analyses. Birth interval was calculated between the birth date of the individual and that of his or her immediately older sibling. Categorical variables were created for birth order (1, 2, . . . , 6+) and maternal age at birth (5-year groups from 15–19 to 45–49 years). Information on parental occupational socioeconomic position (SEP) was derived from the PHCs 1960–1980.

BirthData comprised boys and girls born 1973–1987 with information on birth weight, birth length, and gestational age from the MBR. In the entire dataset we had 1,365,755 individuals and exclusion of those who were firstborn to their mothers left a sample of 767,384 individuals. We had 14,661 cases (1.9% of the data) of missing or extreme values for gestational age (<29 or >45 weeks) and birth weight (<700 or >6,000 g), which were excluded from the final dataset ( $n = 752,723$ ). For additional analyses, we restricted the sample to those families in which all siblings were born in years 1973–1987 and excluded individuals with birth order more than 5. After exclusion of firstborn to their mothers and extreme values, 443,324 individuals remained of which 345,986 belonged to the status of second born. Sex-specific  $z$  scores (i.e., mean = 0 and SD = 1) for birth weight and length were calculated from both the full and restricted samples. Birth weight for birth length  $z$  score was used as a measure of relative weight.

For AdultData, additional information was obtained from the MSCR. Conscription examination, which

TABLE 1. Subjects characteristics at birth according to sex of the preceding sibling, stratified by sex of the individual (full sample)

	Boys		Girls	
	Older brother	Older sister	Older brother	Older sister
Socio demographic				
Birth year	1980.0 (4.4)	1980.0 (4.4)	1980.0 (4.4)	1980.0 (4.4)
Gestational age (weeks)	39.5 (1.7)	39.6 (1.7)	39.6 (1.7)	39.7 (1.6)
Birth order	2.5 (0.8)	2.5 (0.8)	2.5 (0.8)	2.5 (0.8)
Birth interval (years)	4.3 (2.8)	4.3 (2.8)	4.3 (2.8)	4.3 (2.8)
Maternal age (years)	29.4 (4.6)	29.4 (4.6)	29.4 (4.6)	29.4 (4.6)
High SEP (%) fathers/mothers	28.7/19.3	28.6/19.1	28.6/19.2	28.3/18.9
Anthropometrics				
Birth weight (g)	3629.5 (539.8)	3648.0 (539.5)	3495.9 (515.1)	3505.0 (513.9)
Birth length (cm)	50.96 (2.26)	51.03 (2.26)	50.13 (2.16)	50.16 (2.16)
Birth weight (z score)	-0.017 (1.00)	0.018 (1.00)	-0.009 (1.00)	0.009 (1.00)
Birth length (z score)	-0.016 (1.00)	0.018 (1.00)	-0.008 (1.00)	0.008 (1.00)
Birth weight for gestational age (z score)	-0.011 (1.00)	0.011 (1.00)	-0.003 (1.00)	0.003 (1.00)
Birth length for gestational age (z score)	-0.011 (1.00)	0.011 (1.00)	-0.003 (1.00)	0.003 (1.00)
Birth weight for length (z score)	-0.006 (1.00)	0.006 (1.00)	-0.003 (1.00)	0.004 (1.00)
N of observations	200,477	188,178	187,532	176,536

Mean and (standard deviations).  
SEP, socioeconomic position.

predates active military service, was mandatory in Sweden by law for all young male Swedish citizens in our study cohorts. Only males with severe handicap or a chronic disease were exempted from the examination. Conscription examination was carried out in six different centers and measurements were assessed by administrative staff trained for this purpose according to a standard protocol. In this study, we analyzed cohorts born from 1951 to 1976. In the entire data set, we had conscription data available for 1,330,027 men. After exclusion of those who were firstborn to their mothers and had their conscription examination after 1994, the sample was reduced to 520,089 individuals. In addition, to keep the sample age homogenous, men aged less than 17 or more than 20 years at conscription were excluded (6,311 men, 1.2%). During the conscription examination, height and weight were measured in light clothing without shoes. BMI was defined as weight (kg) divided by height squared ( $m^2$ ). We had 7,012 cases (1.3%) of missing or extreme values for height (<150 or >210 cm), weight (<40 or >150 kg), and BMI (<15 or >60  $kg/m^2$ ), which were excluded from further analyses. Elbow flexion, hand grip, and knee extension strength were also measured according to a standard protocol. The exact measurement protocol is regarded to be confidential information by the Swedish Defence Recruitment Agency and thus is not revealed. However, there were no systematic differences evident in the mean values of the measures between conscription offices, suggesting that a uniform protocol was used. The values of elbow flexion, hand grip, and knee extension strength in these data were also close to values in a previous study of 31- to 35-year-old Finnish men (Viitasalo et al., 1985). Strength measures varied from 50 to 999 Newton (N), which was the maximum value the test could measure even if a participant was stronger. We had missing strength values for 441 cases (0.08%). In the final data set (AdultData), we had valid measures from all anthropometric traits on 506,326 men. AdultData was restricted with the same criteria used for BirthData, which left a sample of 425,955 second through fifth born men, of which 303,302 were second born. This study has

been approved by the Ethical Review Board, Stockholm, Sweden.

### Statistical analyses

To study the association between the sex of preceding sibling and the anthropometrics of subsequent offspring, multiple linear regression analyses were performed. Measurements of body size and muscle strength were used as dependent variables, and the sex of the previous sibling as an independent variable. In BirthData, regression analyses were performed separately by the sex of later born sibling. Adjustments were carried out for birth year, birth interval, birth order, and maternal age in model 1, and additionally for gestational age in model 2. For adult anthropometrics (AdultData), model 1 adjusted for birth year, conscription age and center, and model 2 added controls for birth order, birth interval and maternal age. Since BMI was not normally distributed and thus log-transformed, the estimated regression coefficients for this variable can be interpreted as percentage changes ( $\log BMI \times 100 = \% \text{ change}$ ). Next, we used the restricted samples to analyze whether having at least one older brother (not necessarily the just preceding sibling) compared to considering only the preceding brother modifies the associations. We considered all second through fifth born children and for each child we counted the number of preceding brothers and dichotomized the variable (prior boys = 1, no prior boys = 0). Finally, we repeated the analyses taking into account only the second born. Standard errors and *P* values were adjusted for clustering of brothers within families. All models were estimated using Stata/IC 12.0 (StataCorp, College Station, TX).

## RESULTS

### Characteristics of the participants

Table 1 presents the characteristics of the participants at birth (BirthData) according to the sex of the preceding sibling. Mean values for birth year, birth order, birth interval and maternal age did not differ by the sex of

TABLE 2. Descriptive statistics for young adult men according to sex of the preceding sibling (full sample)

	Older brother	Older sister
Socio demographic		
Conscription age (years)	18.2 (0.4)	18.2 (0.4)
Birth year	1965.5 (6.6)	1965.5 (6.6)
Birth order	2.6 (1.0)	2.6 (1.1)
Birth interval (years)	3.8 (2.3)	3.8 (2.3)
Maternal age (years)	28.8 (5.1)	28.8 (5.1)
High SEP (%) fathers/mothers	31.0/14.8	30.9/14.8
Anthropometrics		
Height (cm)	179.15 (6.5)	179.22 (6.5)
Weight (kg)	69.86 (10.4)	69.68 (10.3)
BMI (kg/m <sup>2</sup> )	21.74 (2.9)	21.67 (2.8)
Elbow flexion strength (N)	391.5 (84.6)	391.9 (84.2)
Hand grip strength (N)	618.1 (97.8)	618.9 (97.2)
Knee extension strength (N)	574.4 (118.7)	575.1 (117.6)
N of observations	260,263	246,063

Mean and (standard deviations).

BMI, body mass index; SEP, socioeconomic position.

the previous sibling or that of the subsequent one. Gestational age was slightly lower for both boys and girls when born after a brother (39.5 and 39.6 weeks, respectively) versus a sister (39.6 and 39.7 weeks, respectively). The proportion of high parental SEP (nonmanual workers at higher and middle level), despite very similar, was slightly lower for those born after a sister. Mean birth weight and length were lower in females and both boys and girls presented a smaller size at birth (weight, length and weight for length) when born after a brother. For young adult men (AdultData), sociodemographic characteristics did not vary with the sex of the previous sibling (Table 2). Regarding anthropometrics, men born after a brother presented slightly higher weight and BMI, and lower height and muscle strength than those born after a sister. Cohen's *d* effect size calculated from the means and SDs was very small for all analyzed traits ( $d < \pm 0.035$ ), being particularly low for muscle strength ( $d < 0.010$ ).

### Regression analysis

Linear regression analyses assessing the association between the sex of the preceding sibling and the body size at birth of the subsequent child are presented in Table 3. The unadjusted model showed that boys born after a brother were, on average, 18 g lighter and 0.08 cm shorter than those born after a sister ( $P < 0.001$ ). Adjustments for birth year, birth order, birth interval and maternal age did not change the magnitude of the differences. However, the adjustment for gestational age attenuated the associations to 10 g and 0.04 cm ( $P < 0.001$ ). Together with the results from the gestational age *z* scores, this indicates that part of the lower mean birth weight and length of individuals born after a brother is due to a shorter gestation compared with those born after a sister.

In addition, birth weight for length *z* scores showed a substantially weaker association compared to birth weight *z* scores (0.012 vs. 0.034 in model 1, respectively,  $P < 0.001$ ), suggesting that large part of the association between the sex of the previous sibling and birth weight of the subsequent offspring is explained by birth length. Although associations followed the same pattern in girls,

they were considerably weaker than for boys in all cases. Girls born after a brother presented, on average, 9 g and 0.03 cm less than those born after a sister, but the effect was nonsignificant after the adjustment for gestational age. Analyses carried out on the restricted sample showed that the magnitude of the associations slightly increased when the conditions of having at least one older brother or including only second born children were considered.

Table 4 shows the results for young adult men. Individuals born after a brother were, on average, 0.16 kg heavier and had 0.3% higher BMI than those born after a sister. The associations with height and muscle strength showed the opposite direction, but the magnitude was very small. Having at least one older brother or considering only second born children slightly increased some of the associations. Finally, regression analyses for all outcomes (both at birth and young adulthood) were additionally adjusted for parental SEP, but since regression coefficients did not change, this covariate was not included.

## DISCUSSION

The findings from this population based study of more than half a million Swedish individuals showed that, although the magnitude of the associations is in general very small, the sex of the preceding sibling is related to the anthropometric variation of the subsequent offspring, both at birth and young adulthood. Since we aimed to analyze these relationships in the whole population (2nd–16th born), and more restrictions in the inclusion criteria (2nd–5th born or only 2nd born children) showed similar associations, the discussion will be based on the full samples.

We found that boys and girls born after a brother had a reduced birth weight of 18 g (~0.5%) and 9 g (~0.3%), respectively, compared to those born after a sister. These results are consistent with several previous studies conducted on other populations (Blanchard and Ellis, 2001; Cote et al., 2003; Magnus et al., 1985; Nielsen et al., 2008; Rickard, 2008; Trotnow et al., 1976). For example, Rickard (2008) observed that those individuals born after a brother were 9% lighter at birth than those born after a sister. In a study carried out in 2,022 children from Quebec (Cote et al., 2003), newborn males with only older brothers weighed 87 g less than those with only older sisters, whereas females had a nonsignificant reduction of 14 g. In a register-based study of 545,839 second to fourth born children from Denmark (Nielsen et al., 2008), having one or two older brothers, respectively, was associated with a reduction in birth weight of 29 and 38 g on later born boys and of 17 and 21 g on later born girls compared with later born siblings with no brothers. Our findings are in accordance with these two studies (Cote et al., 2003; Nielsen et al., 2008) in determining a smaller reduction in later born girls than in boys, although providing the smallest effect sizes yet reported. The discrepancies in the magnitudes across studies might in part be explained by differences in terms of origin, cohort, sample size, selection criteria and treatment of data. In contrast to all these previous studies, however, Vernier et al. (2010) found that boys born after a preceding male pregnancy (based on "conceptuses of gravida's previous pregnancies" and not on "sibships") weighted 27 g more than those born after a female pregnancy, and that girls born after a preceding



TABLE 4. Regression coefficients and standard errors for the differences in adult anthropometrics according to sex of the preceding sibling (reference category sister)

	Full sample				Restricted sample					
	Unadjusted		Model 1		Model 2		Model 1		Model 2	
	At least one older brother		At least one older brother		At least one older brother		At least one older brother		At least one older brother	
Weight (kg)	0.17 <sup>c</sup> (0.03)	0.17 <sup>c</sup> (0.03)	0.16 <sup>c</sup> (0.03)	0.17 <sup>c</sup> (0.03)	0.17 <sup>c</sup> (0.03)	0.16 <sup>c</sup> (0.03)	0.15 <sup>c</sup> (0.03)	0.19 <sup>c</sup> (0.04)	0.19 <sup>c</sup> (0.04)	
Height (cm)	-0.07 <sup>c</sup> (0.02)	-0.07 <sup>c</sup> (0.02)	-0.07 <sup>c</sup> (0.02)	-0.07 <sup>c</sup> (0.02)	-0.07 <sup>c</sup> (0.02)	-0.17 <sup>c</sup> (0.02)	-0.10 <sup>c</sup> (0.02)	-0.09 <sup>c</sup> (0.02)	-0.09 <sup>c</sup> (0.02)	
lgBMI × 100	0.31 <sup>c</sup> (0.03)	0.31 <sup>c</sup> (0.03)	0.31 <sup>c</sup> (0.03)	0.31 <sup>c</sup> (0.04)	0.31 <sup>c</sup> (0.04)	0.39 <sup>c</sup> (0.04)	0.31 <sup>c</sup> (0.04)	0.36 <sup>c</sup> (0.04)	0.37 <sup>c</sup> (0.04)	
Elbow flexion strength (N)	-0.41 (0.24)	-0.40 (0.24)	-0.40 (0.24)	-0.41 (0.26)	-0.38 (0.26)	-0.009 (0.26)	-0.53 (0.27)	-0.43 (0.30)	-0.39 (0.30)	
Hand grip strength (N)	-0.80 <sup>b</sup> (0.27)	-0.76 <sup>b</sup> (0.27)	-0.74 <sup>b</sup> (0.28)	-0.78 <sup>b</sup> (0.30)	-0.78 <sup>b</sup> (0.30)	-1.30 <sup>c</sup> (0.30)	-1.07 <sup>b</sup> (0.31)	-0.68 (0.35)	-0.67 (0.35)	
Knee extension strength (N)	-0.75 <sup>a</sup> (0.33)	-0.77 <sup>a</sup> (0.32)	-0.75 <sup>a</sup> (0.32)	-0.75 <sup>a</sup> (0.35)	-0.78 <sup>a</sup> (0.35)	-2.27 <sup>c</sup> (0.36)	-1.06 <sup>b</sup> (0.37)	-0.38 (0.41)	-0.40 (0.41)	

For the restricted sample, “at least one older brother” included individuals with one older brother ( $n = 208,944$ ) and with more than one older brother ( $n = 42,435$ ).

Model 1. Adjusted for birth year, conscription age, and conscription centre.

Model 2. Additionally adjusted for birth order, birth interval, and maternal age.

<sup>a</sup>  $P < 0.05$ .

<sup>b</sup>  $P < 0.01$ .

<sup>c</sup>  $P < 0.001$ .

female pregnancy weighted 48 g more than those born after a male pregnancy. As for birth weight, we observed that boys and girls born after a brother presented a slight decrease in birth length of 0.08 and 0.03 cm, respectively compared to those born after a sister. A trend towards a shorter length for boys with older brothers (51.40 cm) versus older sisters (51.68 cm) was also detected in Quebec children (Cote et al., 2003), but differences were nonsignificant. We additionally showed that a great part of the association between sex of the previous sibling and birth weight of the subsequent child is explained by birth length. In line with this, it has been reported that the associations between birth weight and adult height almost disappeared when adjusting for birth length (Sørensen et al., 1999), and that birth length might be a better predictor of adult height and weight than birth weight (Eide et al., 2005). It is noteworthy, however, that in the present study the associations are significant because of a very large sample size, that is, in smaller samples some of the differences would not become statistically significant.

According to the observations of Nielsen et al. (2008), adjustment for important determinants of birth weight such as birth year, birth interval, birth order and maternal age, did not change the magnitude of the associations, suggesting a fundamental biologic mechanism. Also in agreement with Nielsen et al. (2008), we found that part of the difference in mean birth weight is explained by a shorter gestation in individuals born after a brother than a sister, particularly in girls, for which the effect disappeared in our study. As reviewed by Ellison (2003), the establishment of a pregnancy is sensitive to energetic conditions, but the continuation of it appears to be highly buffered from variation in energetic conditions. This can, however, affect both the duration of gestation and the birth weight of the resulting offspring. A Danish study reported that the delivery of boys, in comparison with the delivery of girls, was associated with an increased risk of stillbirth in subsequent pregnancies and that the risk increment was greater among boys (Nielsen et al., 2010). Thus, the relationship between the sex of the preceding sibling and alterations of gestation needs further attention.

Since producing sons versus daughters is energetically more demanding to the mother owing to their higher size at birth (Hindmarsh et al., 2002; Loos et al., 2001) and their higher energy requirements during gestation (Tamimi et al., 2003) and lactation (Butte et al., 2000; da Costa et al., 2010; Sellen, 2007), the direction of our results—lower birth size and weight after a preceding brother versus a preceding sister—is in line with evolutionary expectations of reproductive costs in humans. Particularly boys seemed to be influenced more from an elder brother compared to girls, which is also expected by the theory since boys require more resources for growth than girls. Two recent studies showed that the energy content of a mother’s breast milk is greater for male infants than for females (Fujita et al., 2012; Powe et al., 2010). In addition, Fujita et al. (2012) observed that economically sufficient mothers in rural Kenya produced richer milk for sons than daughters while poor mothers produced richer milk for daughters than sons. Although these studies are consistent with the Trivers–Willard hypothesis, which predicts the unequal parental investment between males and females depending on maternal condition and offspring reproductive potential (Trivers and Willard, 1973), a recent study based on

milk composition found no support for this hypothesis (Quinn, 2013). It must be noted that it is difficult to illustrate that energy savings a mother would gain by constraining the growth in 18 g (or less) would be sufficiently beneficial for this “strategy” to become genetically encoded and physiologically expressed as an adaptation, through evolutionary time. Based on the magnitude of our findings, however, it is unlikely that the differences in birth weight and length are evolutionary relevant in modern context. We observed that having at least one older brother (not necessarily the just preceding sibling) compared to considering only the preceding brother do not decrease the magnitude of the associations, which could be suggesting that the mechanisms involved possess memory. A plausible physiologic explanation suggested in other studies is the maternal immune responses against H–Y antigens (e.g., Blanchard and Ellis, 2001; Nielsen et al., 2008). Pregnancies with boys lead to maternal immune responses against H–Y antigens, which through inflammatory processes might cause insufficient placental function and thus a reduced birth weight of younger siblings (Bartha et al., 2003). As proposed by Nielsen et al. (2010), this mechanism might also explain the smaller effect observed in girls in such a way that the H–Y reaction might lose specificity with time and become directed towards nonsex-specific proteins on the fetus that have achieved immunogenicity due to the inflammatory process initiated by the anti-H–Y reaction.

In this large population of young adult men, we previously observed that birth order was associated with height, BMI and muscle strength (Jelenkovic et al., 2013; Myrskylä et al., 2013). In this study we show that young men born after a brother were 0.16 kg (~0.3%) heavier, 0.22 kg after adjustment for height, than those born after a sister. In contrast, Rickard (2008) observed that individuals born after a brother were 7% lighter, and that this difference was caused by difference in height. In that sample of 79 men and women (Rickard, 2008), those born after a brother were 2.4% shorter. In our population, however, the effect was considerably lower: being born after a brother was associated with a reduction in height of 0.07 cm (0.04%) only. To our knowledge, no other study has analyzed the relationship between sex of the preceding sibling and BMI or muscle strength. We showed that BMI is 0.3% greater and hand grip and knee extension strength lower (<1 N) in those men born after a brother compared to those born after a sister. As for birth size the majority of associations were not materially affected by adjustments, suggesting a biological effect of sex of the preceding sibling on the subsequent offspring. Therefore, although the direction of the associations suggests that men with an older brother are slightly disadvantaged for anthropometric traits related to human male reproductive fitness (Ellison, 2003; Kuzawa, 2007), which agree with the decreased lifetime reproductive success detected for those individuals born after a brother in the preindustrial Finnish population (Rickard et al., 2007), the magnitude is unlikely to be sufficiently large to have a meaningful impact on male fitness in modern western societies.

Since individuals born after a brother showed reduced birth weight, and decreased height and muscle strength and increased weight and BMI in young men, our findings are in line with the DoHAD hypothesis (Barker, 1998); but again, the small effect sizes (e.g., 18 g difference in birth weight) are unlikely to have biological rele-

vance for health. On the other hand, it is important to mention the role of testosterone, the primary male sex hormone. Testosterone stimulates the growth and maintenance of sexually dimorphic traits such as height, lean mass, and strength and has shown reduced concentrations in individuals born small. In fact, the associations between birth weight and these testosterone-sensitive traits are substantially stronger in males (Kuzawa, 2007). Finally, it has also been hypothesized that an intergenerational phenotypic “inertia” allows the matriline to recalibrate expenditure in response to predictive information that is made more reliable as a result of averaging across generations (Kuzawa, 2007). Thus, further research is required to elucidate biological pathways through which these associations might arise.

This study has several strengths. The main advantage is the large sample size, which allows us to detect very small effects or even lack of association and thus helps to cope with publication bias that potentially favors the publication of unrealistically large effect sizes. In addition, this is the first study to investigate the long-term consequences of the sex of the preceding sibling on BMI and muscle strength of the subsequent offspring. Moreover, since military conscription was mandatory during the study period, participation bias due to selection does not exist. However our study also has some limitations. First, our adult sample included only men and thus our results cannot be generalized to women. Second, although military conscription was mandatory during the study period, severe disability or a severe chronic disease was a valid reason to be exempted, thus our cohort represents mainly healthy Swedish men at baseline. Third, since this is a register-based study, we can only speculate about the biological mechanisms behind the observed associations.

Regardless of the underlying mechanism, our study illustrates the existence of an association between sex of the preceding sibling and anthropometrics of the subsequent offspring both at birth and young adulthood. Although the magnitude is in general very small, we show that being born after an older brother is associated with reduced birth weight and length but with increased weight and BMI in young adulthood. Thus, although the effect is too weak to be of clinical relevance, these findings have theoretical significance and might help to shed light on the underlying biological mechanisms in future research.

## ACKNOWLEDGMENTS

AJ is supported by a postdoctoral fellowship from the Basque Government’s Department of Education, Universities and Research (DEUI). KS is supported by the Academy of Finland (#266592). SH is supported by The Turku Collegium for Science and Medicine.

## LITERATURE CITED

- Barker DJP. 1998. Mother, babies and health in later life. Edinburgh: Churchill Livingstone.
- Bartha JL, Romero-Carmona R, Comino-Delgado R. 2003. Inflammatory cytokines in intrauterine growth retardation. *Acta Obstet Gynecol Scand* 82:1099–1102.
- Bérubé CH, Festa-Bianchet M, Jorgenson JT. 1996. Reproductive costs of sons and daughters in rocky mountain bighorn sheep. *Behav Ecol* 7:60–68.
- Blanchard R, Ellis L. 2001. Birth weight, sexual orientation and the sex of preceding siblings. *J Biosoc Sci* 33:451–467.

- Brisbois TD, Farmer AP, McCargar LJ. 2012. Early markers of adult obesity: a review. *Obes Rev* 13:347–367.
- Butte NF, Wong WW, Hopkinson JM, Heinz CJ, Mehta NR, Smith EO. 2000. Energy requirements derived from total energy expenditure and energy deposition during the first 2 years of life. *Am J Clin Nutr* 72:1558–1569.
- Cote K, Blanchard R, Lalumiere ML. 2003. The influence of birth order on birth weight: Does the sex of preceding siblings matter? *J Biosoc Sci* 35:455–462.
- da Costa TH, Haisma H, Wells JC, Mander AP, Whitehead RG, Bluck LJ. 2010. How much human milk do infants consume? Data from 12 countries using a standardized stable isotope methodology. *J Nutr* 140(12):2227–2232.
- Dodds R, Denison HJ, Ntani G, Cooper R, Cooper C, Sayer AA, Baird J. 2012. Birth weight and muscle strength: a systematic review and meta-analysis. *J Nutr Health Aging* 16:609–615.
- Eide MG, Oyen N, Skjaerven R, Nilsen ST, Bjerkedal T, Tell GS. 2005. Size at birth and gestational age as predictors of adult height and weight. *Epidemiology* 16:175–181.
- Ellison PT. 2003. Energetics and reproductive effort. *Am J Hum Biol* 15:342–351.
- Fujita M, Roth E, Lo YJ, Hurst C, Vollner J, Kendell A. 2012. In poor families, mothers' milk is richer for daughters than sons: a test of trivers-willard hypothesis in agropastoral settlements in Northern Kenya. *Am J Phys Anthropol* 149:52–59.
- Gluckman P, Hanson M. 2006. *Developmental origins of health and disease*. Cambridge: Cambridge University Press.
- Helle S, Lummaa V. 2013. A trade-off between having many sons and shorter maternal post-reproductive survival in pre-industrial Finland. *Biol Lett* 9:20130034.
- Helle S, Lummaa V, Jokela J. 2002. Sons reduced maternal longevity in preindustrial humans. *Science* 296:1085.
- Hindmarsh PC, Geary MP, Rodeck CH, Kingdom JC, Cole TJ. 2002. Intrauterine growth and its relationship to size and shape at birth. *Pediatr Res* 52:263–268.
- Jelenkovic A, Silventoinen K, Tynelius P, Myrskylä M, Rasmussen F. 2013. Association of birth order with cardiovascular disease risk factors in young adulthood: a study of one million Swedish men. *PLoS One* 8:e63361.
- Kuzawa CW. 2007. Developmental origins of life history: growth, productivity, and reproduction. *Am J Hum Biol* 19:654–661.
- Lawlor DA, Ronalds G, Clark H, Smith GD, Leon DA. 2005. Birth weight is inversely associated with incident coronary heart disease and stroke among individuals born in the 1950s: findings from the Aberdeen children of the 1950s prospective cohort study. *Circulation* 112:1414–1418.
- Loos RJ, Derom C, Eeckels R, Derom R, Vlietinck R. 2001. Length of gestation and birthweight in dizygotic twins. *Lancet* 358:560–561.
- Magnus P, Berg K, Bjerkedal T. 1985. The association of parity and birth weight: testing the sensitization hypothesis. *Early Hum Dev* 12:49–54.
- Marsal K, Persson PH, Larsen T, Lilja H, Selbing A, Sultan B. 1996. Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr* 85:843–848.
- Melanson KJ, McInnis KJ, Rippe JM, Blackburn G, Wilson PF. 2001. Obesity and cardiovascular disease risk: research update. *Cardiol Rev* 9:202–207.
- Myrskylä M, Silventoinen K, Jelenkovic A, Tynelius P, Rasmussen F. 2013. The association between height and birth order: evidence from 652 518 Swedish men. *J Epidemiol Commun Health* 67:571–577.
- Nielsen HS, Mortensen L, Nygaard U, Schnor O, Christiansen OB, Andersen AM. 2008. Brothers and reduction of the birth weight of later-born siblings. *Am J Epidemiol* 167:480–484.
- Nielsen HS, Mortensen LH, Nygaard U, Schnor O, Christiansen OB, Andersen AM. 2010. Sex of prior children and risk of stillbirth in subsequent pregnancies. *Epidemiology* 21:114–117.
- Parsons TJ, Power C, Logan S, Summerbell CD. 1999. Childhood predictors of adult obesity: a systematic review. *Int J Obes Relat Metab Disord* 23:S1–107.
- Phillips DI, Handelsman DJ, Eriksson JG, Forsen T, Osmond C, Barker DJ. 2001. Prenatal growth and subsequent marital status: longitudinal study. *BMJ* 322:771.
- Powe CE, Knott CD, Conklin-Brittain N. 2010. Infant sex predicts breast milk energy content. *Am J Hum Biol* 22:50–54.
- Quinn EA. 2013. No evidence for sex biases in milk macronutrients, energy, or breastfeeding frequency in a sample of Filipino mothers. *Am J Phys Anthropol* 152:209–216.
- Rasmussen F, Johansson M. 1998. The relation of weight, length and ponderal index at birth to body mass index and overweight among 18-year-old males in Sweden. *Eur J Epidemiol* 14:373–380.
- Rickard IJ. 2008. Offspring are lighter at birth and smaller in adulthood when born after a brother versus a sister in humans. *Evol Human Behav* 29:196–200.
- Rickard IJ, Russell AF, Lummaa V. 2007. Producing sons reduces lifetime reproductive success of subsequent offspring in pre-industrial Finns. *Proc Biol Sci* 274:2981–2988.
- Risnes KR, Vatten LJ, Baker JL, Jameson K, Sovio U, Kajantie E, Osler M, Morley R, Jokela M, Painter RC, Sundh V, Jacobsen GW, Eriksson JG, Sorensen TI, Bracken MB. 2011. Birthweight and mortality in adulthood: a systematic review and meta-analysis. *Int J Epidemiol* 40:647–661.
- Roff DA, editor. 2002. *Life history evolution*. Sunderland: Sinauer Associates.
- Rogers I, EURO-BLCS Study Group. 2003. The influence of birthweight and intrauterine environment on adiposity and fat distribution in later life. *Int J Obes Relat Metab Disord* 27:755–777.
- Sellen DW. 2007. Lactation, complementary feeding, and human life history. In: Hawkes K, Paine RR, editors. *The evolution of human life history*. Santa Fe: School of American Research Press. p 155–196.
- Silventoinen K, Magnusson PK, Tynelius P, Batty GD, Rasmussen F. 2009. Association of body size and muscle strength with incidence of coronary heart disease and cerebrovascular diseases: a population-based cohort study of one million Swedish men. *Int J Epidemiol* 38:110–118.
- Sørensen HT, Sabroe S, Rothman KJ, Gillman M, Steffensen FH, Fischer P, Sorensen TI. 1999. Birth weight and length as predictors for adult height. *Am J Epidemiol* 149:726–729.
- Tamimi RM, Lagiou P, Mucci LA, Hsieh CC, Adami HO, Trichopoulos D. 2003. Average energy intake among pregnant women carrying a boy compared with a girl. *BMJ* 326:1245–1246.
- Trivers RL, Willard DE. 1973. Natural selection of parental ability to vary the sex ratio of offspring. *Science* 179:90–92.
- Trotnow S, Bregulla K, Flugel K. 1976. Studies on the birthweight and the size of the new-born child with reference to the parity of the mother (author's transl). *Geburtshilfe Frauenheilkd* 36:744–750.
- Vagero D, Modin B. 2002. Prenatal growth, subsequent marital status, and mortality: longitudinal study. *BMJ* 324:398.
- Vernier MC, Mackenzie CJ, Schulzer M, Vernier PR. 2010. Influence of the mother's preceding pregnancies on fetal development and postnatal survival of the neonate, in normal pregnancy. An immunological phenomenon? *Am J Hum Biol* 22:708–715.
- Viitasalo JT, Era P, Leskinen AL, Heikkinen E. 1985. Muscular strength profiles and anthropometry in random samples of men aged 31–35, 51–55 and 71–75 years. *Ergonomics* 28:1563–1574.