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Handgrip Strength: Indications of Paternal Inheritance in Three European Regions

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Background. Handgrip strength is an indicator of overall muscle strength. Poor handgrip strength is a risk factor for disability and mortality. We aimed to investigate the pattern of inheritance of handgrip strength in a sample of parent–offspring pairs from three different European regions in Denmark, France, and Italy.

Methods. In this substudy of the European Challenge for Healthy Aging study, handgrip strength was measured in 290 subjects aged 90 years and older and in one of their offspring.

Results. When all pairs were considered together, parental and offspring handgrip strength were weakly correlated ($r = .16$; $p < .01$). However, paternal–offspring correlation was significantly higher than maternal–offspring correlation ($r = .26$; confidence interval [CI]: 0.11–0.41 versus $r = .03$; CI: −0.14 to 0.19; $p = .04$). This difference was particularly marked for daughters ($r = -.07$; CI: −0.29 to 0.16 for mother–daughter correlation versus $r = .31$; CI: 0.11–0.49 for father–daughter; $p = .01$) compared with sons ($r = .12$; CI: −0.13 to 0.36 for mother–son correlation versus $r = .25$; CI: 0.00–0.46 for father–son; $p = .47$). Father–daughter correlation remained higher than mother–daughter when analyses were performed with 144 nondependent parents ($r = .32$; CI: 0.04; 0.55 versus $r = -.25$; CI: −0.61 to 0.21; $p = .03$). These results were similarly observed in the three regions of the study, where mean levels of handgrip strength strongly differed.

Conclusions. It suggests that age-related effects on functional health among women could be mediated more through the paternal line than the maternal.

Key Words: Handgrip strength—Paternal inheritance—familial transmission—Centenarians—Longevity.

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HANDGRIP strength provides an estimate of isometric strength in the upper extremity. It correlates highly with strength in other muscular groups and is therefore considered as a good indicator of overall muscular strength (1). Several studies have shown that handgrip strength decreases with age from midadulthood onward, reflecting biological decline in muscular strength (2, 3). However, great interindividual variation has been observed in mean level. Poor strength in mid- or late adulthood has been shown to predict functional limitations, disability, and mortality at older ages (4, 5). Handgrip strength is also frequently used as a single or as part of indicators of frailty (6, 7).

Thus, handgrip strength appears to be a convenient and suitable phenotype for identifying environmental and genetic factors influencing mid- to late-life physical functioning (8, 9). The major external factors known to be associated with muscular strength are physical activity, health, and nutritional status (10). Genetic factors also contribute to interindividual differences in handgrip. They were estimated to account for 20—50% of the overall variance (8, 11, 12). These estimates are all based on twin studies, which provide ideal material to assess heritability of a phenotype. Although no gender effect was reported for the heritability coefficient (8), none of these studies examined the extent to which handgrip strength might be transmitted differentially through paternal or maternal line. Assessment of sex-specific patterns of transmission of physical functioning might provide new insight about the factors influencing functional health and its decline at older ages.

In the present work, we aimed to investigate the pattern of inheritance of handgrip strength by analyzing correlations between individuals aged 90 years and older and one of their offspring in three different European regions in Denmark, France, and Italy.

Table 1. Distribution of Age, Handgrip Strength and Frequency of Nondependent Subjects in the Parental Nonagenarian–Centenarian Sample

		Denmark		France		Italy		Total	
Age (y)		*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)
	Men	51	96.7 (95–104)	43	97.6 (94–107)	59	98.3 (93–104)	153	97.6 (93–107)
	Women	34	100.0 (99–106)	57	99.4 (90–108)	46	98.9 (93–106)	137	99.4 (90–108)
Handgrip (kg)		*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*
	Men	51	24.78 ± 7.16	43	19.88 ± 6.78	59	14.66 ± 5.68	153	19.50 ± 7.76
	Women	34	13.21 ± 4.69	57	10.75 ± 5.48	46	9.60 ± 4.43	137	10.98 ± 5.11
Nondependent (%)	Men		68.6		51.2		66.1		62.7
	Women		44.1		29.8		34.8		35.0

Note: *SD* = standard deviation.

Materials and Methods

Sampling

A total of 598 long-lived probands (nonagenarians or centenarians) were recruited in three European regions (Southern Denmark, Languedoc-Roussillon in France, and Calabria in Italy) as part of the European Challenge for Healthy Aging Study, which aimed to identify genetic and environmental determinants of longevity. Age criteria for long-lived proband were defined according to sex- and country-specific life expectancy. The lower age limit corresponded approximately to the 5th upper percentile of the age-at-death distribution. From these probands as a starting point, families were recruited including at least a long-lived proband, one of his/her child and one of his/her niece or nephew. One sibling of the long-lived parent, parent of the niece or nephew, was recruited if he/she was alive, aged 90 years and older and willing to participate. As described in previous publications, different strategies for identification and recruitment of the families were used in the three European regions (13, 14).

For the present analysis, we selected all available parent–offspring pairs, that is, either a long-lived proband and his/her child or a sibling and his/her child. Long-lived probands and sibling made the nonagenarian–centenarian parental generation, whereas children and nieces or nephews made the offspring generation. Of 361 available pairs, 290 (ie, 80%) had complete data for handgrip strength measurement and were included. Sixty-six long-lived parents (48 women and 18 men) and 13 (6 women and 7 men) children had missing value for handgrip strength. The main reason for missing data in handgrip strength was bedridden or acute frailty among nonagenarian and centenarian participants. Mean handgrip strength was not different between offspring of pairs included in the study sample and their nonincluded counterparts.

Handgrip Strength Measurement

Handgrip strength was measured with a handgrip dynamometer (Smedley, model 281128; Scandidact, Kvistgaard, Denmark) on the hand of choice using standard method. The maximum value in kilograms of three successive measurements was selected for the analysis.

Measure of Disability

Long-lived parents were classified as being nondependent when they reported to be able to perform the four following activities of daily living tasks: feeding, dressing, transferring, and toileting.

Statistical Analysis

Differences in mean handgrip strength between sex, country, or generation were tested by analyses of variance. Crude Pearson correlation coefficients between children and parents handgrip strength were computed for each country and each type of parent–child pair (mother–daughter, father–daughter, mother–son, and father–son). Analyses of covariance were then performed separately for parents and offspring to estimate effects of sex, age, and country on handgrip strength. Residuals of these two regression models were then used to compute "adjusted" correlation coefficients between parents and offspring. 95% confidence intervals for the correlation coefficients and p values for two-by-two comparisons of the correlations obtained in the different type of parent–child pair were provided after Fisher's Z transformation. All statistical analyses were performed using SAS statistical package software version 9.1 (SAS Institute, Cary, NC).

Results

Handgrip distribution parameters are given in Tables 1 and 2 for a total sample of 290 parent–offspring pairs. As expected, handgrip strength was higher in offspring compared with parental generation ($p < .0001$) and higher in men compared with women ($p < .0001$). Moreover, a clear north–south gradient is observed; Danish had significantly higher handgrip strength compared with French, and French compared with Italian. This trend was consistently observed in each generation and each gender.

Table 2. Distribution of Age, Handgrip Strength and Height in the Offspring Sample

			Denmark		France		Italy		Total
Age (y)		*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)	*n*	Mean (minimum–maximum)
	Men	48	65.8 (54–80)	34	68.8 (54–85)	45	69.1 (59–82)	127	67.7 (54–85)
	Women	37	67.4 (57–83)	66	68.2 (48–82)	60	68.2 (54–78)	163	68.0 (48–83)
Handgrip (kg)		*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*
	Men	48	50.36 ± 7.82	34	41.76 ± 8.16	45	33.42 ± 6.43	127	42.06 ± 10.37
	Women	37	30.13 ± 4.81	66	26.71 ± 4.29	60	20.90 ± 5.10	163	25.35 ± 5.94
Height (cm)		*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*	*n*	Mean ± *SD*
	Men	46	176.6 ± 6.3	34	171.6 ± 5.4	45	165.3 ± 6.1	125	171.2 ± 7.6
	Women	35	164.6 ± 6.5	66	161.9 ± 5.5	59	154.3 ± 5.6	160	159.7 ± 7.1

Note: *SD* = standard deviation.

Assessment of disability among the 290 subjects of the parental generation indicated that 62.7% of the men were classified as nondependent compared with only 35.0% of the women (Table 1).

Associations between parental and offspring handgrip strength in each country and each type of parent–child pair, that is, mother–daughter, mother–son, father–daughter, and father–son are shown in Figure 1. Father–daughter crude correlation coefficients were strong and significant in Denmark (r = .49 ; p = .02) and Italy (r = .47; p = .004). Correlation coefficient was weaker in France (r = .34) and statistical significance was borderline (p = .06). By contrast, mother–daughter correlation coefficients were close to zero in the three countries. Daughters' strength was not associated to maternal strength.

Correlation coefficients between parent and offspring handgrip strength were then computed using the residuals of the regression of handgrip strength on age, sex, and country in both parental and offspring sample (Table 3). A weak but significant association between parent and offspring handgrip strength was observed when considering all pairs (r = .16; p < .01). However, the extent of the association differed according to the type of pair. Paternal–offspring correlation (r = .26) was significantly higher than maternal–offspring correlation (r = 0.03; Table 3). This difference was particularly marked for daughters (r = −.07 for mother–daughter correlation versus r = .31 for father–daughter) compared with sons (r = .12 for mother–son correlation versus r = .25 for father–son). Comparison of correlation coefficients according to the offspring indicated similar level of association between parents and either type of child (0.19 for sons and 0.13 for daughters).

Similar results were obtained when the analyses were restricted to 144 nondependent parents (48 women and 96

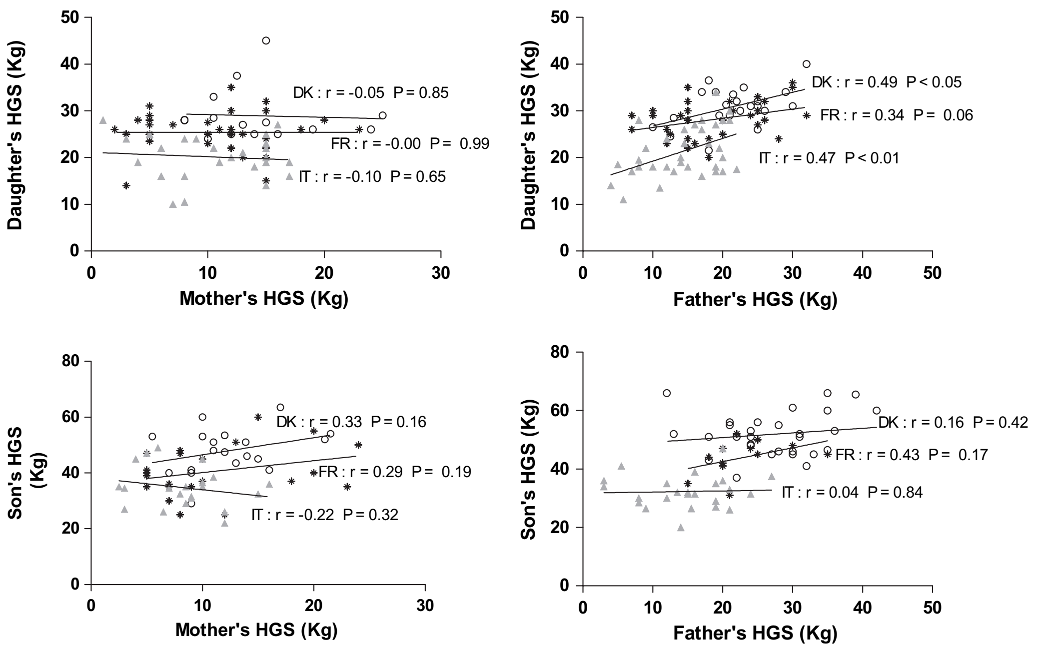

Figure 1. Correlations between parental and offspring handgrip strength (HGS) in each European region. Open circle, Southern Denmark (DK); asterisk, Languedoc-Roussillon, France (FR); shadowed triangle, Calabria, Italy (IT). *Note:* r = Pearson correlation coefficient.

Table 3. Correlation Coefficients between Parents' and Offspring's HGS

	Maternal HGS	Paternal HGS	*p* Value*	Parental HGS
Daughters' HGS				
n	75	88		163
ρ	−.07	.31	.01	.13
95% CI	−0.29 to 0.16	0.11–0.49		−0.02 to 0.28
p	.52	.003		.10
Sons' HGS				
n	62	65		127
ρ	.12	.25	.47	.19
95% CI	−0.13 to 0.36	0.001–0.46		0.02–0.36
p	.35	.047		.03
p Value†	.35	.67		.57
Offspring's HGS				
n	137	153		290
ρ	.03	.26	.04	.16
95% CI	−0.14 to 0.19	0.11–0.41		0.05–0.27
p	.74	.0008		.005

Notes: Correlation coefficients were computed from the residuals of the regression of HGS on age, sex, and country to account for these covariables. 95% CI = 95% confidence interval after Fisher's *Z* transformation; ρ = Pearson correlation coefficient; HGS = handgrip strength; *n* = number of pairs used to compute the correlation; *p* = *p* value for association between HGS in each paired sample; *SD* = standard deviation.

* *p* Value for comparison of the correlation coefficients between paternal and maternal samples.

† *p* Value for comparison of the correlation coefficients between sons' and daughters' samples.

Table 4. Correlation Coefficients between Nondependent Parents and Offspring HGS

	Maternal HGS	Paternal HGS	p Value*	Parental HGS
Daughters' HGS				
n	21	50		71
ρ	−.25	.32	.03	.12
95% CI	−0.61 to 0.21	0.04–0.55		−0.11 to 0.35
p	.27	.02		.30
Sons' HGS				
n	27	46		73
ρ	.41	.31	.66	.33
95% CI	0.02–0.68	0.02–0.55		0.11–0.52
p	.03	.03		.004
p Value†	.03	.97		.19
Offspring's HGS				
n	48	96		144
ρ	.12	.31	.28	.25
95% CI	−0.17 to 0.39	−0.11 to 0.48		0.09–0.40
p	.41	.002		.002

Notes: Correlation coefficients were computed from the residuals of the regression of HGS on age, sex, and country to account for these covariables. 95% CI = 95% confidence interval after Fisher's *Z* transformation; ρ = Pearson correlation coefficient; *n* = number of pairs used to compute the correlation; *p* = *p* value for association between HGS in each paired sample.

* *p* Value for comparison of the correlation coefficients between paternal and maternal samples.

† *p* Value for comparison of the correlation coefficients between sons' and daughters' samples.

men; Table 4). The lack of association between mothers and daughters in contrast to positive association for father–daughter pairs was confirmed. Comparison of correlation coefficients between offspring and parents of either sex, indicated higher association for paternal strength, but the difference did not reach statistical significance, partly due to an increased correlation between mothers and sons.

To address the issue of an association of handgrip strength with height, correlation coefficients were also computed with offspring height as an additional confounding factor. Similar results were found (data not shown).

Discussion

The present work investigated patterns of inheritance of handgrip strength in three different European regions. Analysis of correlation between parental and offspring handgrip strength indicated an overall weak association. However, the strength of the correlation depended on the type of parent–offspring pair. Indeed, offspring handgrip strength was significantly correlated with paternal but not maternal handgrip strength. This result was particularly striking in daughters for whom handgrip strength was strongly associated with fathers' handgrip strength, whereas no association was observed with mothers. Moreover, this result was similarly observed in the three regions implicated in the study, where mean levels of handgrip strongly differed.

Our observation of a positive correlation between parent and offspring handgrip strength is consistent with several twin studies indicating that handgrip strength was in part heritable. Genetic factors were estimated to account for 20%–50% of the overall variance (8, 11, 12). Two of these studies have focused either on female or male twins and could thus, not assess for gender effect (11, 12). The third study, including both men and women, found no clear difference in heritability estimates between gender (8). Our observation of differential parental effect on offspring handgrip strength, suggesting a paternal inheritance, is unique; we are not aware of any previous publication investigating parent–offspring association for this trait. The positive correlations in handgrip strength arise from shared characteristics between parents and children, which may include genetic factors but also a wide range of nongenetic shared characteristics such as lifestyle, exercise habits, wealth, social status, and others. Conversely, other kind of factors may contribute to weaken the association. Frailty could be one of these. Indeed, handgrip strength measurement among very frail or heavily disabled persons may not reflect their "intrinsic," "normal" muscular strength. The higher prevalence of frailty and disability among long-lived women could be an explanation for the weak association of maternal handgrip strength with their offspring strength. Indeed, it is well known that although women live longer, they experience greater disability than men of the same age (15, 16). The gender difference in disability is also observed in our study population. First, 48 mother–offspring pairs of the 361 available pairs (ie, 13%) had to be excluded from the analysis because the long-lived women were too weak to be tested for handgrip strength, whereas only 5% of the long-lived men were excluded. Second, among the 290 pairs included in the analysis, only 35% women were classified as nondependent compared with 62.7% in men. To test if disability could account for the gender-related effect in the transmission, correlation analyses were assessed in a subsample including only nondependent parents. The lack of association between mothers' and daughters' handgrip strength was confirmed. Thus, the higher prevalence of disability among long-lived women cannot explain the gender effect in the association.

We are not aware of similar observations based on other functional phenotypes. Indication of paternal inheritance have however been reported for another age-related trait, generally considered as a reliable marker of biological age; that is, telomere length. Indeed, two independent studies investigated the pattern of inheritance of telomere length and found a significant correlation between offspring and paternal telomere length, whereas no association was found with maternal telomere length (17, 18). This pattern might suggest sex chromosome–linked inheritance or influence of epigenetic mechanisms, such as differential imprinting.

We could wonder if lifespan exhibits the same inheritance pattern. Studies on longevity do not display consistent nor conclusive results on sex-specific patterns of inheritance, but peculiar association between fathers' and daughters' lifespan were repeatedly reported as indicating either weaker or stronger associations compared with other intrafamilial relations (19). Further examination of the methods used in these studies showed that weak father–daughter correlations for lifespan were generally found when early mortality of the offspring was included in the analysis, whereas strong correlations applied to studies focusing on late adult mortality (19). A family-based study in northern Sweden also reported a stronger effect of paternal versus maternal effect of longevity on offspring's lifespan (20). Although, this pattern needs confirmation, it potentially brings support to the existence of a paternal inheritance of the mechanisms involved in aging at advanced ages.

Several aspects of our analyses warrant comment. First, the present study describes the pattern of association of handgrip strength between individuals aged 90 years and older and one of their offspring. These results may not apply to the general population with younger parent–offspring pairs. Second, we were not able to control for correlation of handgrip strength between spouses because only one parent was included. In most cases, the spouse of the long-lived parent has already died. We had to assume that correlations between spouses were similar for couples with a long-lived man or with a long-lived woman. Another limitation to our study is that the child included in the pair was not chosen randomly. The child enrolled was often the one who took care of the parent. Although this situation could have modulated the strength of the association, it is difficult to formulate specific hypotheses for this effect.

In conclusion, this study reports original findings of a gender-dependent effect in the association between parental and offspring handgrip strength. Although pending confirmation, these results suggest that age-related effects on functioning among women would be mediated more through the paternal than the maternal line. Further investigation might provide new insight about the factors influencing functional health and its decline at older ages.

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