Do Children of Long-Lived Parents Age More Successfully?

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Background. Long-lived individuals are rare and may be selected in part for the genetic factors that promote successful aging. The children of long-lived parents may therefore age more successfully than the children of short-lived parents.

Methods. We used three major cross-sectional populationbased surveys to study the association of parental longevity with successful aging in offspring. The measures of aging were hand-grip strength, cognitive performance (Mini Mental State Examination and a cognitive composite score), self-reported diseases, and self-rated health.

Results. For every additional 10 years the parents lived, their children's grip strength increased by 0.32 kg (95% CI = 0.00-0.63), Mini Mental State Examination score by 0.20 points (95% CI = 0.03-0.37), and cognitive composite score

by 0.24 points (95% CI = 0.07–0.40). A 10-year increment of parental life was associated with a reduction by approximately 0.20 in the adjusted odds ratio for their children having each of the following conditions: diabetes; hypertension; ischemic heart disease; heart failure; stroke; or fair, poor, or very poor self-rated health. Almost all the effects were seen solely in the cohort of 70+-year-olds, but not among middle-aged or nonagenarian subjects.

Conclusions. Parental life span is positively associated with the children's physical and cognitive functioning and avoidance of some of the common chronic diseases. However, the effects are small and are seen among offspring who are elderly, but not among the middle-aged or the oldest old. (EPIDEMIOLOGY 2002;13:334–339)

Key words: aging, twins, oldest-old, parents, longevity, hand strength, cognition.

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A aintenance of high physical and cognitive functioning and avoidance of disease and disability are central to "successful" aging.¹ Ever since Rowe and Kahn¹ introduced the concept of successful aging, a number of mainly environmental predictors (eg, education, income, social network, physical activity, and smoking status) have been shown to influence the components of successful aging.^{2,3} In recent years, researchers have also begun to investigate the contribution of genetic factors to successful aging.^{4–6} Studies of elderly twins suggest that genetic factors account for a substantial proportion of the variance in

physical⁷ and cognitive^{8,9} functioning, and a moderate proportion of variance in life span.¹⁰ An important genetic component to some of the major diseases of aging, such as cardiovascular diseases,¹¹ diabetes and impaired glucose tolerance,¹² and some cancers (breast, prostate, and colorectal),¹³ has also been found. Long-lived individuals are rare and may be selected in part for the genetic factors that promote successful aging. The children of long-lived parents may therefore age more successfully than the children of short-lived parents. Whatever the mechanism, not much is known about the interplay between parental longevity and the aging of offspring. Here we use three major Danish nationwide surveys of middle-aged, elderly, and oldest-old people to study the association of parental life span with the respondents' physical and cognitive functioning, as well as specific illnesses.

Methods

Sample

The sample comprised participants in three nationwide population-based surveys: the Study of Middle-Aged Danish Twins (MADT),¹⁴ the Longitudinal Study

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of Aging Danish Twins—3rd wave (LSADT),¹⁵ and the Danish 1905 Cohort Survey (1905),¹⁶ which have all been described in detail previously. In brief, participants in the MADT and LSADT studies were identified in the Danish Twin Register,¹⁷ and participants in the 1905 survey were identified in the Danish Civil Registration System, both nationwide, population-based registers that are continuously updated. The eligible participants in the MADT study represented a random sample of 120 twin pairs from each of the 22 birth cohorts in 1931-1952. The eligible participants in the LSADT were Danish twins age 70 years and older in 1999, and those in the 1905 study were all Danes born in 1905. All surveys were conducted in periods of 3-6 months in 1998–1999. The participation rates were 83.1% in the MADT (N = 4,314), 69.9% in the LSADT (N = 2,709), and 62.8% in the 1905 cohort study (N = 2,262). All three studies used a highly comparable structured interview, which was home-based and included physical and cognitive testing performed by lay interviewers from the Danish National Institute of Social Research. All interviewers had substantial experience interviewing the elderly and furthermore completed a detailed training program by a physician and were closely monitored during the interview periods.

All studies were approved of by the Danish scientific ethical committees, and all participants provided informed consent.

Parental Age at Death

Information on parental age at death was obtained during the interview in the LSADT and 1905 studies and through a mailed questionnaire (1996–1998) before the MADT study. The twins within the intact pairs (both twins in a pair participating) reported their father's age at death with a correlation of 0.99 (95%) confidence interval [CI] = 0.99-0.99 in the MADT study and 0.96 (95% CI = 0.95-0.96) in the LSADT study, and their mother's age at death with a correlation of 0.98 (95% CI = 0.98-0.99) in the MADT and 0.98 (95% CI = 0.97-0.98) in the LSADT study. In the MADT and LSADT studies both twins in a pair were excluded if they differed by 5 or more years in their report of either their father's or mother's age at death (N = 244 individuals). The average of the fathers' and mothers' ages at death, as well as fathers' and mothers' ages at death separately, was used in the analyses.

Physical Functioning

Hand-grip strength, which has been shown to reflect overall muscle strength,¹⁸ was measured with a hand dynamometer (Smedley's dynamometer TTM, Tokyo). We identified the maximum value of three measures with each hand in the LSADT and MADT studies, and of three measures with the preferred hand in the 1905 study. Participants with fewer than three attempts, or with a difference of 20 kg or more between two measures, were excluded from this analysis (N = 268).

Cognitive Functioning

Integrated in the interview was a series of cognitive tests including the Mini Mental State Examination (MMSE) (in the LSADT and the 1905 studies only), a test of fluency (number of animals named in 1 minute), forward and backward digit span, and a modified 12word learning test. The scores of the four latter tests were standardized and summed to form a cognitive composite score that was used in the analysis.

Health

In all surveys the participants were asked whether a physician had ever told them that they suffered from various diseases. Participants who answered "Yes, previously" or "Yes, currently" were subsequently asked to confirm that this was a diagnosis made by a doctor, before the answer was accepted as valid.

Data Analysis

We divided participants into five groups by average parental age at death (<54, 55-64, 65-74, 75-84, and 85+) and compared these groups with regard to physical and cognitive functioning as well as a number of selfreported diseases. Several potential confounding characteristics (body mass index, smoking habits, alcohol consumption, and education) were confirmed to be unrelated to parental life span. Both parents were deceased for about half of the participants in the MADT study. In the LSADT study only 15 participants had one parent still alive, and in the 1905 cohort study none of the participants had living parents. All measures were age- and sex-adjusted by subtracting age (in 5-year intervals) and sex-specific means from the actual scores.¹⁹ The residuals are presented in the figures. In all subsequent analyses, participants with parents who on average died before age 54 were excluded (N = 243) as a result of the large proportion of deaths not related to the biology of aging (eg, accidents and suicides) before this age. After this, the effect of increasing the mean parental age at death by 10 years was assessed by entering the categorized value as a continuous measure in a multivariate linear regression model for continuous outcomes (grip strength and cognitive tests) or in a logistic regression model for dichotomous outcomes (self-reported diseases), controlling for the age and sex of the participants. A model with parental age at death as a continuous variable and a model with parental age at death in 10-year groups gave virtually the same results and comparable Bayesian information criteria. To account for the nonindependence of the observations on twins, twins from pairs in which both participated were ana-

	MADT	1	LSADT		1905		
	Mean \pm SD	N	Mean \pm SD	Ν	Mean \pm SD	N	
Age of participants % females Father's age at death* Mother's age at death* Mean parental age at death*† Grip strength‡ MMSE score Cognitive composite score§	$56.9 \pm 6.3 \\ 49.0 \\ 72.5 \pm 12.0 \\ 73.6 \pm 13.3 \\ 73.9 \pm 9.4 \\ 38.1 \pm 12.4 \\ - \\ 4.6 \pm 3.5$	4,314 2,116 3,231 2,466 2,136 4,148 4,309	$78.3 \pm 6.0 \\ 57.8 \\ 74.4 \pm 12.8 \\ 76.0 \pm 15.2 \\ 75.3 \pm 10.1 \\ 26.6 \pm 9.6 \\ 25.8 \pm 5.4 \\ 1.5 \pm 3.5 \\ \end{cases}$	2,709 1,565 2,403 2,463 2,281 2,288 2,565 2,481	$\begin{array}{c} 93 \pm 0 \\ 74.2 \\ 74.5 \pm 14.1 \\ 73.8 \pm 16.1 \\ 74.1 \pm 10.8 \\ 16.0 \pm 6.7 \\ 21.4 \pm 6.0 \\ 0.0 \pm 3.6 \end{array}$	2,262 1,678 1,877 1,981 1,835 1,485 1,798 1,784	

TABLE 1. Basic Characteristics of 9,285 Participants in Three Large Danish Population-Based Studies

MADT = Study of Middle-Aged Danish Twins; LSADT = Longitudinal Study of Aging Danish Twins—3rd wave; 1905 = Danish 1905 Cohort Study; MMSE = Mini Mental State Examination (in LSADT and 1905 studies only).

* Individuals in a twin pair are excluded if they reported the father's (n = 152), mother's (n = 140), or both parents' (n = 244) age at death in the MADT and LSADT studies with 5 or more years' difference.

† For participants with both parents dead, average of fathers and mothers age at death.
‡ Maximum of at least three examinations with less than 20-kg difference between two measures.

A composite measure of test for fluency, forward and backward digit span, and a modified 12-word learning test.

lyzed as clusters of two in the multivariate models. Thirteen twins born in 1905 participated in both the 1905 and the LSADT survey. The data from both surveys of these participants were used in the analyses because they were so few and sampled with an interval of 6 months.

Results

Table 1 shows the basic characteristics of the participants in the three surveys. Table 2 shows the number of participants across categories of parental longevity. At least one parent was still alive among 1,920 (20.7%), and information regarding age at death was missing among 887 (9.6%, Table 2). In the MADT study, the twins in 1,978 (99.2%), 1,581 (99.2%), and 1,306 (98.9%) intact pairs reported their father's, mother's, or both parents' age at death within ± 4 years. In the LSADT, the twins in 473 (88.6%), 490 (89.4%), and 428 (80.8%) intact pairs reported their father's, mother's, and both parents' age at death within ± 4 years.

Mean parental age at death was only modestly associated with physical and cognitive functioning, as seen in Figures 1–3 and Table 3. For each 10-year increase in parental life span, average grip strength increased by only 0.32 kg (95% CI = 0.00-0.63) (Table 3). The effect was seen only in the LSADT cohort (mean age mid-70s), but not among the twins who were middleaged (MADT), or the cohort of nonagenarians (1905). Likewise, the relation of cognitive functioning to parental age at death was seen solely in the LSADT cohort; each 10-year increase in parental age at death was associated with an increase of 0.20 (95% CI = 0.03-0.37) MMSE points and 0.24 (95% CI = 0.07-0.40) cognitive composite points (Table 3). The analyses used for Table 3 were repeated using parental age at death as a continuous variable in the multivariate linear regression models. The coefficients were, when multiplied by 10, virtually identical to the ones in Table 3 (results not shown).

A number of self-reported diseases were associated with parental life span (Table 4). Again the effect was mainly present in the LSADT cohort. In this cohort the age- and sex-adjusted odds ratios (ORs) for having either previous or current diabetes, hypertension, ischemic heart disease, heart failure, or stroke each decreased by roughly 0.20 for every 10-year increase in mean parental age at death (Table 4). Also, the odds for having fair, poor, or very poor self-rated health were associated with parental age at death: OR = 0.8 (0.7 to 0.9) in both the MADT and LSADT cohorts by 10-year increase in parental age at death. Pulmonary disease, cancer, osteoarthritis, and osteoporosis were not associated with pa-

TABLE 2. Number of Participants (Percentages) in Three Large Danish Population-Based Studies Stratified by Mean Parental Age at Death

	Mean Parental Age at Death (Both Parents Dead)																	
	<	54	55	-64	65-	-74	75-	-84	85	5+	One Parent Alive		Two Parents Alive		Unknown		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
MADT LSADT 1905	82 85 89	1.9 3.1 3.9	257 282 240	6.0 10.4 10.6	680 657 514	15.8 24.3 22.7	889 991 666	20.6 36.6 29.4	256 464 326	5.9 17.1 14.4	1,389 15 0	32.2 0.6 0.0	516 0 0	12.0 0.0 0.0	245 215 427	5.7 7.9 18.9	4,314 2,709 2,262	100 100 100

MADT = Study of Middle-Aged Danish Twins; LSADT = Longitudinal Study of Aging Danish Twins-3rd wave; 1905 = Danish 1905 Cohort Study.



FIGURE 1. Grip strength by parental longevity (age- and sex-adjusted residuals) among 9,285 participants in three surveys: the Study of Middle-Aged Danish Twins (MADT), the Longitudinal Study of Aging Danish Twins—3rd wave (LSADT), and the Danish 1905 Cohort Survey (1905).

rental life span in any cohort (Table 4). In the 1905 cohort, parental life span was not associated with any disease or self-rated health. In the MADT cohort there was a borderline association of parental life span with hypertension and stroke, but not with any other disease (Table 4). Because the associations observed between parental life span and stroke, ischemic heart disease, and heart failure could reflect confounding from the association also seen with hypertension and diabetes, we subsequently used a model for stroke, ischemic heart disease, and heart failure including hypertension and diabetes only in the LSADT sample. The point esti-



FIGURE 2. Cognitive composite score by parental longevity (age- and sex-adjusted residuals) among 9,285 participants in three surveys: the Study of Middle-Aged Danish Twins (MADT), the Longitudinal Study of Aging Danish Twins— 3rd wave (LSADT), and the Danish 1905 Cohort Survey (1905).



FIGURE 3. MMSE score by parental longevity (age- and sex-adjusted residuals) among participants in two surveys: the Longitudinal Study of Aging Danish Twins—3rd wave (LSADT), and the Danish 1905 Cohort Survey (1905).

mates from these models for these three diseases were virtually unaltered.

Discussion

The relationship between long-lived parents and successful aging has been reported in one previous paper.²⁰ Vaillant studied a cohort of 188 males age 65 years who had been recruited in 1940–1942 as healthy students from the top half of their classes in college (Harvard University). When the 16% with longest maximum ancestral longevity were compared with the 16% with shortest ancestral longevity, long-lived ancestors predicted "sustained health" on a crude 1–5 scale.

A number of issues in our study need to be addressed. The information about parental life span was based on self-report from the participants, which could be subject to error, although it is reassuring that the twins within the intact pairs reported their parents' age at death with high correlations. The proportion able to report the parental age at death (± 3 years) compared with death certificates has previously been found in Sweden to be between 82.8% and 86.5% for fathers and 86.7% and 90.2% for mothers.²¹

To estimate the effect of potential misclassification of parental age at death, we repeated the analyses excluding those in which the interviewers stated that the interview was completed with difficulties (of any kind and severity) (N = 1,324). The point estimates after this restriction were very similar to those reported here, although the confidence intervals widened.

We report here the results of the analyses using the average of the mothers' and fathers' age at death as the covariate of interest. This approach enabled us to use the

	Average Change by 10-Year increase in Average Parental Age at Death									
	M	IADT	LS	ADT	1905					
	Average	95% CL	Average	95% CL	Average	95% CL				
Physical function Maximum hand-grip strength, kg*	0.14	-0.27, 0.55	0.32	0.00, 0.63	-0.02	-0.35, 0.30				
MMSE score† Cognitive composite score‡	-0.06	-0.25, 0.13	0.20 0.24	0.03, 0.37 0.07, 0.40	0.00 -0.05	-0.31, 0.32 -0.24, 0.15				

TABLE 3. Physical and Cognitive Functioning Among 9,285 Participants in Three Large Danish Population-Based Studies in Relation to Parental Age at Death

The numbers are average change in the respective measure by 10-year increase in mean parental age at death with 95% confidence intervals in brackets. The coefficients are adjusted for age and sex. MADT = Study of Middle-Aged Danish Twins; LSADT = Longitudinal Study of Aging Danish Twins-3rd wave; 1905 = Danish 1905 Cohort Study; MMSE = Mini Mental State Examination.

* Maximum of at least three examinations with less than 20 kg difference between two measures.

† Only cohorts from the Danish 1905 Cohort Study and the Longitudinal Study of Aging Danish Twins.

‡ A composite measure of test for fluency, forward and backward digit span, and a modified 12-word learning test.

information from those with two long-lived parents, a group that could be expected to experience "successful aging." To get an impression of parental-specific effects, we also analyzed the effects of fathers' and mothers' ages at death separately. However, the results were not systematically different between the two (results not shown). The results from the participants with one or two parents still alive were censored from the analyses. As seen in Table 2, the number of participants omitted for this reason was only considerable in the MADT cohort and may have contributed to the lack of association between parental age at death and the outcomes in this cohort.

Participants who did not provide information on parental age at death were more cognitively impaired than the rest (Figures 2-3). These participants were also approximately 10 years older (mean 81.2 ± 14.2) than participants without missing information (mean 70.9 \pm 15.8). The direction of the potential bias introduced by the lack of information from these participants is not evident.

When analyzing MMSE score as the outcome, we used methods that rely on a normal distribution of the data. Because the MMSE score is highly skewed, we repeated the regressions using bootstrap methods.²² The confidence intervals differed only in the third decimal place (data not shown).

We found that parental life span is associated with physical and cognitive functioning and health in the cohort of 70+ year olds. Age-related differences in functioning and health among middle-aged individuals may not be large enough to detect a small effect of parental longevity. In the nonagenarian 1905 cohort, it would have been surprising if parental life span had had an impact, because reaching an age of 92+ may in itself be regarded as successful aging.

In conclusion, we found that at older ages parental life span is positively associated with physical and cognitive functioning and avoidance of some of the quantitatively important diseases. However, the overall effects are small in absolute terms and are seen only among

TABLE 4. Self-Reported* Diseases and Health Among 9,285 Participants in Three Large Danish Population-Based Studies in Relation to Parental Age at Death

	Odds Ratio for Each 10-Year Increase in Average Parental Age at Death									
	Ν	MADT	Ι	SADT	1905					
	OR	95% CI	OR	95% CI	OR	95% CI				
Diabetes Pulmonary disease† Hypertension Ischemic heart disease‡ Heart failure Stroke Cancer excluding skin Osteoarthritis Osteoporosis	0.86 0.92 0.88 0.90 0.71 1.03 0.90 0.97	0.64-1.14 0.78-1.09 0.77-1.00 0.72-1.07 0.72-1.12 0.50-1.00 0.75-1.40 0.79-1.03 0.69-1.36	0.82 0.96 0.86 0.82 0.81 0.76 1.00 1.05 0.99	0.69-0.96 0.85-1.09 0.78-0.96 0.73-0.94 0.70-0.93 0.64-0.90 0.84-1.41 0.95-1.16 0.82-1.20	1.04 0.93 0.92 0.90 0.96 0.90 1.04 1.02 0.98	0.85-1.27 0.80-1.08 0.81-1.03 0.78-1.03 0.85-1.10 0.76-1.07 0.87-1.25 0.92-1.14 0.83-1.16				

Values are age- and sex-adjusted odds ratios and 95% confidence intervals in the respective measure by 10-year increase in mean parental age at death. * Participants were asked if a physician ever had told them that they suffered from any of the mentioned diseases

MADT = Study of Middle-Aged Danish Twins; LSADT = Longitudinal Study of Aging Danish Twins-3rd wave; 1905 = Danish 1905 Cohort Study. Asthma and/or chronic bronchitis

‡ Angina and/or acute myocardial infarction

the elderly (mean age mid-70s), but not among the middle-aged or the oldest old.

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