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GENERAL BIOLOGY

Maternal Age and Lifespan of Offspring

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The purpose of this study was to test the hypothesis that the lifespan of offspring decreases as maternal age increases because of the age-related accumulation of genetic load. Recently, this problem has become of interest due to the development of the mitochondrial theory of aging. According to this theory, mitochondrial DNA, which is inherited through the maternal line, is the primary target of oxidative damage and the site of age-related accumulation of the corresponding lesions [1]. Evidently, this problem is important from both the theoretical (testing the mitochondrial theory of aging and lifespan) and social points of view (possible consequences of the current increase in maternal age, which have been widely discussed [2]).

To solve this problem, we collected and analyzed genealogical data on Russian and foreign nobility (lines of the Belosel'skii-Belozerskii, Volkonskii, Vyazemskii, Golitsyn, Dolgorukov, Kropotkin, Obolenskii, Romanov, Shakhovskoi, Sheremet'ev, and other families) [3–17]. A total of 120 genealogical sources, which we listed earlier [18], were analyzed. As a result, we created a computer database containing information on the birth and death dates for children and their mothers. To ensure that the statistical data was comparatively homogeneous and unbiased, we used only data on people who were born in the 18th and 19th centuries, so that none of them were still living. In order to exclude the effects of high child mortality and violent death at a young age, we calculated the lifespan only for offspring over 30 years old. We analyzed data on a total of 4428 sons, 2547 daughters, and their mothers.

Table 1 shows the results of this analysis. An increase in maternal age from 15–19 to 40–49 years did not affect the lifespan of sons. Conversely, the lifespan of daughters born to mothers over 40 years old decreased substantially (Table 1). Lifespans of daughters born to mothers younger and older than 40 years (67.52 ± 0.34 and 63.98 ± 1.55 years, respectively) differed by 3.6 ± 1.6 years; the difference was statistically significant ($t = 2.26$; $p < 0.05$).

When discussing the obtained results, we should take into account that the population of mothers might be heterogeneous. To bear a child at the age of 40–49 years, the woman had to have a genotype that allowed her (1) to live until this age and (2) to be able to bear and bring up a child at this age. If the high viability of 40- to 49-year-old mothers were inherited (at least partly) by their offspring, this trait might entirely compensate for (mask) the damaging effect of the age-related accumulation of genetic load in mothers. Therefore, in order to study the "pure" effect of maternal age, we had to analyze as homogenous a sample of mothers as possible. These mothers had to have a long lifespan (e.g., no less than 70 years).

Therefore, we analyzed the data on "long-lived" mothers, i.e., those who lived 70 years or longer. Table 2 shows the results of this analysis. We compared data on the children born to young long-lived mothers and those born to all young mothers (Tables 2 and 1, respectively). The comparison demonstrated that the offspring of long-lived mothers had a slightly longer lifespan. This partly confirmed the suggestion on the heterogeneity of the general population of mothers and their offspring. However, offspring of long-lived mothers also exhibited the aforementioned pattern: maternal age did not affect the lifespan of sons; however, daughters born to mothers over 40 years old had a decreased lifespan (Table 2). The lifespan of daughters born to long-lived mothers when these women were younger or older than 40 (69.73 ± 0.48 and 65.19 ± 2.36 years, respectively) differed by 4.5 ± 2.4 years; the difference was statistically significant ($t = 1.88$, $p < 0.05$). Therefore, the decreased lifespan of daughters born to older mothers could not be explained by the social consequences of an early maternal death, because the same pattern was observed for long-lived mothers.

The mutation load is accumulated stochastically; therefore, the adverse effect of advanced maternal age was expected to be seen only in some daughters. In this case, this effect had to decrease as the affected daughters were "rejected." The data shown in Table 3 confirm

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Table 1. The relationship between the lifespan of adult (over 30 years old) offspring and maternal age

Maternal age, years	Sons		Daughters	
	number	mean lifespan ± standard error, years	number	mean lifespan ± standard error, years
15–19	264	60.8 ± 0.9	164	67.6 ± 1.3
20–24	1254	61.7 ± 0.4	702	66.9 ± 0.6
25–29	1360	62.3 ± 0.4	751	68.9 ± 0.6
30–34	917	61.4 ± 0.5	522	66.5 ± 0.8
35–39	454	61.7 ± 0.7	293	67.2 ± 1.0
40–44	153	61.0 ± 1.2	98	64.4 ± 1.7
45–49	26	63.2 ± 2.6	17	61.1 ± 3.9

Table 2. The relationship between the lifespan of adult (over 30 years old) offspring of long-lived (70 years or longer) mothers and maternal age

Maternal age, years	Sons		Daughters	
	number	mean lifespan ± standard error, years	number	mean lifespan ± standard error, years
15–19	87	61.5 ± 1.6	67	71.2 ± 1.9
20–24	556	63.6 ± 0.6	307	68.4 ± 0.9
25–29	632	63.0 ± 0.6	380	71.5 ± 0.9
30–34	442	61.7 ± 0.8	256	68.3 ± 1.0
35–39	247	63.3 ± 0.9	157	69.6 ± 1.3
40–44	71	62.6 ± 1.7	50	65.9 ± 2.6
45–49	10	61.9 ± 4.0	9	61.4 ± 6.1

Table 3. The relationship between the lifespan of long-lived (70 years or longer) offspring and maternal age

Maternal age, years	Sons		Daughters	
	number	mean lifespan ± standard error, years	number	mean lifespan ± standard error, years
15–19	80	77.4 ± 0.7	90	80.7 ± 0.8
20–24	434	77.8 ± 0.3	356	79.8 ± 0.4
25–29	511	77.7 ± 0.3	423	81.5 ± 0.4
30–34	312	78.7 ± 0.4	262	80.4 ± 0.4
35–39	143	78.5 ± 0.6	152	81.0 ± 0.6
40–44	46	78.5 ± 0.9	45	79.6 ± 1.2
45–49	10	76.2 ± 1.2	4	82.8 ± 4.2

this suggestion: the effect of maternal age was not observed in the daughters who lived to be 70 years old.

Note that this study was the first to analyze the long-term effects of maternal age on the lifespan of offspring. Almost all earlier studies focused on the early effects of maternal age on offspring. These were usually classical congenital malformations, including Down's syndrome (trisomy 21), Klinefelter's syndrome (genotype XXY), Edwards syndrome (trisomy 18), Patau syndrome (trisomy 13), etc. [19, 20]. Conversely, this study analyzed the long-term effects of maternal age on the lifespan of the general population of "essentially healthy" people, thus initiating a new stage of research in this field.

The sex specificity of the effect of maternal age on the lifespan of offspring deserves special consideration.

Daughters, but not sons, exhibited a decrease in lifespan with an increase in the maternal age; this phenomenon requires further study. One possible explanation for the absence of the maternal-age effect in adult sons is that males underwent a stronger "rejection" (i.e., had a higher mortality) in early childhood and even during embryogenesis [21].

The results obtained indicate that a special research program on lifespan should be established for a deeper insight into this problem. For example, it is extremely important to discriminate between the maternal and paternal effects. There is a strong correlation between the maternal and paternal ages (with the paternal age usually being slightly higher); therefore, it is difficult to determine whose age (maternal or paternal) actually affects the lifespan of offspring. Our earlier studies demonstrated that the paternal-age effect was the same as the maternal-age one, i.e., an increase in paternal age caused a decrease in the lifespan of daughters [18], but not sons [18, 22]. Discriminating between the maternal-age and paternal-age effects and ultimately testing the predictions of the mitochondrial theory of aging will require accumulation, processing, and analysis of tens of thousands of genealogical records. The accomplishment of this large-scale study will require a considerable expenditure of resources. However, the expenditures will be justified, because the human reproductive age is increasing, and it is important to know the delayed results of this trend.

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REFERENCES

1. Wallace, D.C., *Proc. Natl. Acad. Sci. USA*, 1994, vol. 91, pp. 8739–8746.
2. Gosden, R. and Rutherford, A., *Brit. Med. J.*, 1995, vol. 311, p. 1585.
3. *Dvoryanskie rody Rossiiskoi Imperii, Tom 1: Knyaz'ya* (Noble Families of the Russian Empire, vol. 1: Princes), Dumin, S.V., Ed., St. Petersburg: Vesti, 1993.
4. *Dvoryanskie rody Rossiiskoi Imperii* (Noble Families of the Russian Empire), Dumin, S.V., Ed., St. Petersburg: Vesti, 1995, vol. 2.
5. Ferrand, J., *Les familles princières de l'ancien Empire de Russie*, 1979, vol. 1.
6. Ferrand, J., *Les familles princières de l'ancien Empire de Russie*, 1982, vol. 2.
7. Ferrand, J., *Les familles princières de l'ancien Empire de Russie*, 1982, vol. 3.
8. Ferrand, J., *Les familles comtales de l'ancien Empire de Russie en émigration*, 1982, vol. 1.
9. Ferrand, J., *Les familles comtales de l'ancien Empire de Russie en émigration*, 1983, vol. 2.
10. Schakhovskoy, D., *Societe et Noblesse Russe*, 1978, vol. 1.
11. Schakhovskoy, D., *Societe et Noblesse Russe*, 1979, vol. 2.
12. Schakhovskoy, D., *Societe et Noblesse Russe*, 1982, vol. 3.
13. Schakhovskoy, D., *Societe et Noblesse Russe*, 1982, vol. 4.
14. Ikonnikov, N.F., *La Noblesse de Russie*, Paris, 1932–1964.
15. *Genealogisches Handbuch des Adels*, von Hueck, W., Ed., Limburg an der Lahn: C.A. Starke, 1987, vol. 13.
16. Tolstoy-Miloslavsky, D., *The Tolstoy's Genealogy and Origin*, Alicante, 1991.
17. Kotzebue, R., *History and Genealogy of the Kotzebue Family*, Paris: Hervas, 1984.
18. Gavrilov, L.A., Gavrilova, N.S., Evdokushkina, G.N., *et al.*, *Longevity Rep.*, n.d., vol. 10, pp. 7–15.
19. Vogel, F. and Motulsky, A.G., *Human Genetics: Problems and Approaches*, Berlin: Springer, 1986, 2nd edition. Translated under the title *Genetika cheloveka*, 3 vols., Moscow: Mir, 1989.
20. Finch, C.E., *Senescence and the Genome*, Chicago: Univ. of Chicago Press, 1990.
21. Gavrilov, L.A. and Gavrilova, N.S., *The Biology of Life Span: A Quantitative Approach*, Chur, Switzerland: Harwood Academy, 1991.
22. Gavrilov, L.A., Gavrilova, N.S., Snarskaya, N.P., *et al.*, *Dokl. Akad. Nauk*, 1995, vol. 341, no. 4, pp. 566–568.