Short Report

Effect of Seasonal Programming on Fetal Development and Longevity: Links with Environmental Temperature

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ABSTRACT This study examined the effect of birth season on fetal development and longevity using two independent databases of all Greek citizens that were born (total: 516,874) or died (total: 554,101) between 1999 and 2003. We found significantly increased birth weight, gestational age, and longevity in individuals born during the autumn and winter seasons of the year. These individuals also demonstrated statistically significantly lower prevalence rates for fetal growth restriction and premature birth. Furthermore, we found that increased temperature at birth was associated with adverse effects on fetal development and longevity. In conclusion, our results show strong effects of season of birth on fetal development and longevity mediated, at least in part, by environmental temperature at time of birth. Am. J. Hum. Biol. 21:214–216, 2009. © 2008 Wiley-Liss, Inc.

The fragile biochemical equilibrium of the human intrauterine environment is significantly influenced by environmental factors (Murray et al., 2000) with considerable effects on fetal growth and infant development (Flouris et al., 2005b; Hille et al., 2007). Although stimuli in early postnatal life also play an important role, such insults can result in permanent structural, functional, and metabolic changes which can lead to physiological or metabolic 'programming' of the newborn with negative effects on longevity (Flouris et al., 2005a; Hille et al., 2007; Murray et al., 2000). Indeed, different reports from around the globe suggest an association between the season of birth and longevity (Garilov and Garilova, 1991; Huntington, 1938). Yet, there is considerable controversy as to which periods of the year are associated with favorable health outcomes (Garilov and Garilova, 1991; Huntington, 1938). Relatively recent studies in Europe and Gambia found that humans born during the autumn and winter seasons demonstrate increased birth weight and longevity compared to those born during the remaining periods of the year (Doblhammer and Vaupel, 2001; Moore et al., 1997; Vaiserman et al., 2002). Yet, only few large populations have been investigated hitherto (Doblhammer and Vaupel, 2001), while the effect of 'seasonal programming' on fetal development requires further confirmation. In this light, the primary objectives of the present investigation were to examine whether season of birth influences fetal development and longevity in all Greek citizens that died or were born between the years 1999 and 2003. Given the proposed link between climate conditions in infancy and adult health (Lawlor et al., 2006), a secondary objective of this study was to examine the effect of temperature at birth on fetal development and longevity in these populations.

MATERIALS AND METHODS

Data

Two databases were used to fulfill the purposes of this study. The first database included sex, exact date of birth, birth weight, and gestational age for all Greek citizens born between the years 1999 and 2003 (total: 516,874; males: 553,656; females: 527,519) and mean air temperature during the month of birth. The second database included sex as well as exact dates of birth and death for all Greek citizens that died between the years 1999 and 2003 (total: 554,101; males: 293,566; females: 260,535) and mean air temperature during the year of birth. All human data were extracted from the National Birth and Death Registry of Greece developed from original hospital records, while information on deceased individuals was obtained from original birth and death certificates. No personal information was obtained for any of the participants included in either of the databases. The air temperature data were obtained from the National Meteorological Service via stations distributed throughout the Greece. The study conformed to the standards set by the Declaration of Helsinki and was approved by the ethical review board of the University of Thessaly, Greece.

Statistical analyses

General log-linear analysis was used to examine the effects of season of birth and sex on the number of births per season and the number of deaths per season. MANOVA incorporating eta squared effect size estimate followed by post-hoc t-tests incorporating a Bonferoni adjustment were used to assess the effects of season of birth and sex on birth weight, gestational age, and longevity. Chi-square tests were used to detect differences in the probability of premature birth and fetal growth restriction based on season of birth, following a recategorization of the original gestational age data into term normal (i.e., $\geq$37 weeks) and premature (i.e., $<$37 weeks) infants, and of the birth weight data into low (i.e., $<$2500 g) and normal (i.e., $\geq$2500 g) birth weight. Correlation coefficients were calculated amongst the mean air temperature during the month of birth, birth weight, and gestational age (for the infants) as well as between the mean air tempera-

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TABLE 1. Mean(SD) and MANOVA with accompanying post-hoc tests for longevity of deceased individuals as well as birth weight and gestational age of infants for each season and for the entire year

	Time period	Males	Females	Entire cohort
Longevity (years)	Winter	73.29 (16.09)[b]	79.21 (14.18)[b]	76.05 (15.52)
	Spring	70.96 (17.42)[a,b]	76.98 (15.49)[a,b]	73.72 (16.83)[a]
	Summer	70.86 (17.55)[b]	77.44 (15.41)[b]	73.93 (16.91)
	Autumn	72.99 (16.45)[a,b]	79.35 (13.66)[a,b]	76.03 (15.51)[a]
	Year Mean	72.36 (16.70)[b]	78.60 (14.38)[b]	75.29 (15.96)
Birth weight (g)	Winter	3323.09 (553.27)[b]	3205.63 (518.97)[b]	3271.63 (540.77)
	Spring	3206.91 (558.65)[a,b]	3077.45 (532.76)[a,b]	3144.54 (550.15)[a]
	Summer	3208.45 (547.87)[b]	3082.17 (528.03)[b]	3147.11 (542.01)
	Autumn	3311.11 (555.07)[b]	3184.41 (529.54)[b]	3249.43 (546.47)[a]
	Year Mean	3264.62 (553.66)[b]	3137.16 (527.52)[b]	3202.90 (544.89)
Gestational age (weeks)	Winter	38.86 (1.67)	38.88 (1.60)	38.87 (1.63)
	Spring	38.18 (1.69)[a]	38.20 (1.67)[a]	38.19 (1.68)[a]
	Summer	38.18 (1.67)	38.20 (1.66)	38.19 (1.67)
	Autumn	38.81 (1.75)[a]	38.82 (1.76)[a]	38.82 (1.76)[a]
	Year Mean	38.51 (1.69)	38.52 (1.67)	38.51 (1.68)

MANOVA statistically significant ($P < 0.05$) main effect of sex on birth weight and longevity. MANOVA statistically significant ($P < 0.05$) main effect of birth season for all three variables. No statistically significant sex x birth season interaction effect ($P > 0.05$).
[a]Value significantly different ($P < 0.05$) from previous birth season.
[b]Value significantly different ($P < 0.05$) between sexes for the same time period.

TABLE 2. Prevalence rates (CI) and chi-square test results of fetal growth restriction (i.e., low birth weight) and premature births for each season and for the entire year

	Time period	Males	Females	Entire cohort
Low Birth Weight (<2500 g)	Winter	0.071 (0.002)[a,b]	0.090 (0.002)[a,b]	0.080 (0.001)[a]
	Spring	0.081 (0.002)[b,c]	0.099 (0.002)[b,c]	0.090 (0.002)[c]
	Summer	0.080 (0.002)[b]	0.102 (0.002)[b,c]	0.091 (0.002)
	Autumn	0.074 (0.002)[b,c]	0.095 (0.002)[b,c]	0.084 (0.002)[c]
	Year Mean	0.086 (0.001)[b]	0.096 (0.001)[b]	0.086 (0.001)
Premature (<37 weeks)	Winter	0.054 (0.002)[a,b]	0.050 (0.002)[a,b]	0.052 (0.001)[a]
	Spring	0.064 (0.002)[b,c]	0.062 (0.002)[b,c]	0.063 (0.001)[c]
	Summer	0.063 (0.002)	0.062 (0.002)	0.062 (0.001)
	Autumn	0.059 (0.002)[b]	0.054 (0.002)[b,c]	0.056 (0.001)[c]
	Year Mean	0.059 (0.001)[b]	0.057 (0.001)[b]	0.059 (0.001)

[a]Value in winter significantly different ($P < 0.05$) from autumn.
[b]Value significantly different ($P < 0.05$) between sexes for the same time period.
[c]Value significantly different ($P < 0.05$) from previous Birth Season.

ture during the year of birth and longevity (for the deceased individuals). To ensure that possibly discovered differences in birth weight were not consequences of earlier gestational age, all analyses incorporating birth weight were repeated using standardized birth weight for gestational age (i.e., birth weight/gestational age). The level of significance was set at $P < 0.05$, except for post-hoc tests in which a Bonferroni adjustment was applied.

RESULTS

Initial analyses incorporating case categorization into months demonstrated common patterns based on the different seasons of the year. Hence, all data were re-analyzed using categorization for winter (i.e., December–February), spring (i.e., March–May), summer (i.e., June–August), and autumn (i.e., September–November) seasons of the year based on date of birth. General log-linear analysis showed no main effects of season on the number of births per season ($P = 0.11$) as well as the number of deaths per season ($P = 0.09$). Statistically significant main effects of sex on longevity ($P < 0.001$; eta squared = 0.09) and birth weight ($P < 0.001$; eta squared = 0.08), as well as of birth season on longevity ($P < 0.001$; eta squared = 0.12), birth weight ($P < 0.001$; eta squared = 0.14) and gestational age ($P < 0.001$; eta squared = 0.12) were detected (Table 1). Post-hoc tests demonstrated that individuals born during the autumn and winter had increased birth weight, gestational age, and longevity compared to those born in the remaining seasons of the year. Chi-square comparisons (Table 2) revealed that the prevalence rates of fetal growth restriction and premature birth were statistically lower ($P < 0.05$) for the infants born during the autumn and winter seasons.

Mean air temperature during the month of birth in the infant database correlated with birth weight and gestational age at $r = -0.218$ ($P < 0.001$) [males: $r = -0.217$ ($P < 0.001$); females: $r = -0.218$ ($P < 0.001$)] and $r = -0.210$ ($P < 0.001$) [males: $r = -0.208$ ($P < 0.001$); females: $r = -0.211$ ($P < 0.001$)], respectively. Mean air temperature during the year of birth in the deceased individuals database correlated with longevity at $r = -0.667$ ($P < 0.001$) [males: $r = -0.623$ ($P < 0.001$); females: $r = -0.701$ ($P < 0.001$)].

Finally, all analyses incorporating standardized birth weight for gestational age revealed results similar to those including only birth weight as a parameter.

DISCUSSION

On the basis of the current evidence, yearly season of birth influences fetal development and longevity in Greeks that died or were born between the years 1999 and 2003. According to the detected seasonal programming pattern, individuals born during the colder seasons of the year revealed increased birth weight, longer gestational age, and lived longer than those born in the warmer seasons of the year. Concomitantly, these individuals demonstrated statistically lower risk for fetal growth restriction and premature birth. The warmer part of the year may be relatively advantageous for gestation—and, thus, not for giving birth—because of the favorable seasonal variations in environmental temperature (Wells, 2000) and sunlight exposure (Tustin et al., 2004). On the other hand, during the warmer periods environmental stress may trigger premature delivery more frequently (Lajinian et al., 1997; Porter et al., 1999) leading to the observed earlier gestational age independently to variations in intrauterine conditions during pregnancy. Indeed, we found that increased temperature at birth was associated with adverse effects on fetal development and longevity.

To the authors' knowledge, this is the first study that examined collectively—but independently—the effect of birth season on fetal development and longevity using two independent large samples from the same population. Although the infant birth weight data generally cover a 70-year period after the time when the deceased individuals were born, there is no reason to doubt that the same seasonal patterns would be seen in this previous period. Yet, it is important to highlight that our results suggest associations, not causal relationships, amongst seasonal programming, fetal development and longevity. The present results, would be further strengthened by examining associations between season of birth and cause-specific deaths, by broad causes. Another consideration is the increased infant mortality during the first part of the 20th century which may have left a more robust residual population indicating a positive 'programming', yet this could be the eventuality of detrimental selective effects during early life. Based on the current evidence, it is concluded that Greeks born during the autumn and winter seasons of the year demonstrated increased birth weight, gestational age, and longevity, and showed lower risk for fetal growth restriction and premature birth compared to Greeks born in the remaining seasons of the year. These effects were mediated, at least in part, by environmental temperature. Further research on the effects of seasonal programming on fetal development and longevity should be projected in future studies.

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