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Similar photoperiod-related birth seasonalities among professional baseball players and lesbian women with an opposite seasonality among gay men: Maternal melatonin may affect fetal sexual dimorphism

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ABSTRACT

Based on pre-mid-20th-century data, the same photoperiod-related birth seasonality previously observed in schizophrenia was also recently found in neural-tube defects and in extreme left-handedness among professional baseball players. This led to a hypothesis implicating maternal melatonin and other mediators of sunlight actions capable of affecting 4th-embryonic-week developments including neural-tube closure and left–right differentiation of the brain. Here, new studies of baseball players suggest that the same sunlight actions could also affect testosterone-dependent male–female differentiation in the 4-month-old fetus. Independently of hand-preferences, baseball players ($n=6829$), and particularly the stronger hitters among them, showed a unique birth seasonality with an excess around early-November and an equally significant deficit 6 months later around early-May. In two smaller studies, north-American and other northern-hemisphere born lesbians showed the same strong-hitter birth seasonality while gay men showed the opposite seasonality. The sexual dimorphism-critical 4th-fetal-month testosterone surge coincides with the summer-solstice in early-November births and the winter-solstice in early-May births. These coincidences are discussed and a "melatonin mechanism" is proposed based on evidence that in seasonal breeders maternal melatonin imparts "photoperiodic history" to the newborn by direct inhibition of fetal testicular testosterone synthesis. The present effects could represent a vestige of this same phenomenon in man.

1. Introduction

The present study was guided by and supports in part a "solstitial" hypothesis recently proposed to explain the "birth month phenomenon" in schizophrenia. Mid-20th century and earlier studies found among people with schizophrenia a birth-rate *excess* in late-winter, around late-February, and an equally significant *deficit* 6 months later, around late-August (Torrey et al., 1977, 1997; Marzullo and Boklage, 2011). Based on evidence that schizophrenia is associated with cerebral asymmetry deficits and may in fact represent a failure of left hemisphere dominance over the right hemisphere (Boklage, 1977; Crow et al., 1989; Sommer et al., 2001), we pursued the phenomenon with studies of month of birth and hand preferences among professional baseball players. We found not only a schizophrenia-liability like, February–March birth peak among the least lateralized players (extreme left-handers at the outfield) but also the opposite effects, a schizophrenia-resistance like, August–September birth peak among the most lateralized players (extreme right-handers at first base) (Marzullo and Fraser, 2009). Together, the two effects suggested a strong interaction between month of birth and cerebral lateralization. We had also previously found again the same schizophrenia-like birth seasonality among children born with Neural Tube Defects (NTDs) (Marzullo and Fraser, 2005). This and the hand-preference effects both implicated early-4th-week, neurulating stages of embryogenesis, a narrow time window during which asymmetries are established in the midline organs while the neural tube closes. Based on these convergent elements, we proposed a "solstitial" hypothesis that centered on the coincidence of those 4th-week embryonic stages with the two extremes in the annual photoperiod. The timings were in fact such that a late-February-born baby appeared to "neurulate" under the Summer Solstice (SS) and a late-August born under the Winter Solstice (WS). The solstitial effects were hypothesized to result from pro-oxidant actions of sunlight as mediated by two major blood antioxidants: melatonin, whose secretion by the pineal is suppressed by visible light, and Glutathione (GSH), whose abundance in the skin is cut down by ultraviolet light. Together, the two agents would cause

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the maternal blood antioxidant potential to swing from an antioxidant maximum at the WS to a pro-oxidant maximum at the SS. This invocation of oxidation-reduction followed from evidence that, in addition to occurring together, the processes of neural tube closure and asymmetry development are also both inhibited by pro-oxidant states and promoted by antioxidant states of the maternal blood redox potential (see Marzullo and Boklage, 2011). For example, visceral asymmetry failures (*situs inversus*) and NTDs were found to be the most frequent malformations in infants of mothers with periconceptional oxidant stress due to untreated diabetes (Mills, 1982).

The present study began with the finding of a unique birth seasonality among the same baseball players investigated in our laterality study. Independently of hand preferences or playing position, the players showed as a group a birth-rate *excess* around November and an equally significant *deficit* 6 months later around May. This effect grew in strength together with the hitting strength of the players (see later). Masculinization of the fetus depends upon and has appeared commensurate to (McIntyre, 2006; Breedlove, 2010) a surge of fetal testosterone that peaks around the end of the 4th month (Reyes et al., 1974, Scott et al., 2009). This time point coincides with the SS for early-November births and the WS for early-May births, thus suggesting the possibility that, *mutatis mutandis*, the same solstitial hypothesis proposed to explain anomalies of left–right differentiation in the embryonic brain might also help explain anomalies of male–female differentiation in the fetal central nervous system. This hypothesis is later discussed based on the present results and other findings from animal studies. These indicate that, whether or not acting as antioxidants, maternal melatonin and possibly also maternal GSH may both tend to inhibit fetal masculinization, the former by suppressing fetal testosterone formation and the latter by opposing testosterone action.

Like our earlier studies, the present investigation focused on pre-mid-20th century births, a time of comparatively pristine human exposure to the natural sunlight cycle. As we demonstrated using American data (Marzullo and Boklage, 2011) and others had previously shown based on European data (Roenneberg, 2004), photoperiod-dependent rhythms of general births began to decline in the 1930s *pari passu* with advances in electric illumination and other related indoor attractions. In our baseball study, the handedness effects were no longer significant among players born after 1942. The schizophrenia birth seasonality was also in decline after the 1950s (Suivisaari et al., 2000). By the 1980s, several laboratories even failed to find a winter–summer difference in the blood levels of melatonin among people living mostly indoor, normal lives. They succeeded only after artificially mimicking conditions of normal sunlight exposure (see Marzullo and Boklage, 2011). The present study also sought to more specifically focus on pre-1942 births. This was to avoid deep and prolonged disturbances caused by the sudden events of World War II in the otherwise predictable rhythms of general American and European births.

2. Methods

Baseball player data were obtained as before from a 1986 edition of Reichler's Baseball Encyclopedia (McMillan, NY). For each player, the Encyclopedia provided statistical information in a table illustrated on page 663 in the name of "John Doe". For the present purpose, data recorded from the table included name, date and place of birth, most frequent field position, and lifetime batting average. "Pitchers", listed separately from the "players" in the same Encyclopedia, were not included in the study due to their negligible participation in batting, a central aspect of the study. The birth years ranged from 1836 to 1964, with a median in 1909. The players' monthly birth rates were initially examined in terms of expected rates based on the general male population of 1915–1924. This was the earliest decade with monthly natality data available from a majority of American states (see Marzullo and Fraser, 2009). Biographical data on gay men and lesbian women were initially obtained from a 2001 edition of "Who's Who in Contemporary Gay and Lesbian History" by R. Aldrich and G. Watherspoon (Routledge, London). Those members whose birth month could be found and who had been born in either North America or Europe numbered 270 gays and 66 lesbians. Their birth dates ranged from the late 19th century to 1968 with a median in 1934. Since the United States was the most representated country of origin for both groups, the monthly rates were initially compared to expected rates based on the American general population of 1933–1940. The latter data were obtained from a Vital Statistics "Special Report" that, beginning with 1933, the first year with monthly natality data available from all of the states, sought to minimize extraneous noise and focus on the more purely seasonal components of the American rhythm (Shapiro and Halpin, 1947). Separate male and female reference data for gay and lesbian studies were unnecessary because the M/F sex ratio at birth, which was 1.05 in 1933, is seasonally invariant. Comparable reference data representing the diverse European regions were unavailable. However, comparative studies by Roenneberg and Aschoff (1990) found that general-population birth rhythms, being mainly due to the photoperiod, are essentially similar in North America and Europe at similar latitudes and secular times. More importantly, the ultimate conclusions of this study are not based on comparisons with the general populations but rather on direct comparisons of closely matched gay and lesbian groups.

A second source of contemporary gay and lesbian biographies was the Italian Wikipedia website "Persone GLBT" (http://it.wikipedia.org/wiki/Categoria:PersoneLGBT). This added, respectively, 187 and 77 names to the above lists of American and European gays and lesbians. A birth-year cutoff at 1970 was used in this case both because of the expected loss of seasonality effects after this time and in order to minimize confounders relating to seemingly changing concepts of "gay" and "lesbian" attributes in recent decades (note-1 in Appendix). The few members of each group found to have been born in the southern hemisphere were omitted from the study rather than included with a 6-month shift in the month of birth because the assumption that only physical factors can contribute to the seasonality is likely incorrect. For example, a frequently observed September peak of general births has been seen as a "Christmas" effect resulting from a surge of sexual activity around year-end festivities. Statistical analyses were simply based on the same χ^2 test previously used by others in many schizophrenia studies (*e.g.*, Torrey et al., 1977) and by us in the laterality study (Marzullo and Fraser, 2009).

3. Results

3.1. Baseball players

The initial baseball player results are shown in the upper half of Table 1 and in Fig. 1. Compared to the general male population of 1915–1924, the players ($n=6829$) showed a strong birth seasonality ($p < 10^{-7}$; 11 d.f.) with very significant excesses ($p < 0.01$) in October and November and equally significant deficits particularly in April and May. The black curve in Fig. 1 illustrates this rhythm. A subsequent study was aimed at a possible association between strength of the birth seasonality, based on amplitude of the rhythm, and strength of the players based on lifetime batting averages. This study focused on players born during the 50-year period from 1893 to 1942. The start year was arbitrarily chosen to give the batting average definition and procedures some time to stabilize after their introduction in 1876. The end year, 1942, was chosen to avoid the above mentioned World War II-related disturbances and also because of the post-1940s loss of effects seen in our handedness study. The players' list, now numbering 2872, was first sorted on lifetime batting average (LBA) and then divided into three equal parts, A, B, and C, in decreasing order of mean LBA. Each part was subsequently examined for amplitude of the seasonal rhythm based on the ratio of October–November births to April–May births, or the "October–November/April–May birth ratio." The expected value for this ratio was approximately 1, or 0.98 based on the general male population of 1915–24. The results are presented in Table 2 and Fig. 2.

As indicated in the table, the 1893–1942-born players, with an average LBA of 244, showed as a group an October–November/April–May birth ratio of 1.20, significantly higher than the expected ratio ($p < 0.001$). Among these, the C players, with a below-average mean LBA of 186.4, showed essentially the expected ratio (1.01). The B players, with a near-average mean LBA of 249.8, showed a non-significant but higher than expected ratio of 1.17. The A players, with a well-above-average mean LBA of