Received: 6 January 2020 | Revised: 12 March 2020 | Accepted: 14 March 2020
DOI: 10.1002/ajhb.23417

ORIGINAL RESEARCH ARTICLE

American Journal of Human Biology WILEY

Seasonality and season of birth effect in the UK Biobank cohort

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Abstract

Objectives: Humans live in environments that reduce the impact of seasonal cues. However, studies suggest that many aspects of human biology, such as birth, metabolism, health, and death are still annually rhythmic.

Methods: Using UK Biobank, a large (N = 502 536) population-based resource, we investigated the influence of seasonality on birth rate, basal metabolic rate, health, reaction speed, and sleep. We also investigated the association between season of birth and regional brain volumes, basal metabolic rate, health, reaction speed, and sleep.

Results: Our results showed that annual birth rate peaks in April and May. Individuals had the highest basal metabolic rate in December and January. Poorer subjective general health and slower reaction time were observed in May. Susceptibility to insomnia showed an opposite trend that peaked in autumn and winter. People reported shorter periods of sleep, easier waking, earlier chronotype, more daytime dozing, and napping in summer compared with winter. Our results suggest that season of birth may influence later-life characteristics. We also observed that the effect of season of birth is in the opposite direction of the seasonal rhythm for basal metabolic rate, reaction time, and insomnia. Moreover, our analysis showed that prevalence of allergy is higher among people born in spring compared to autumn.

Conclusions: Overall, our findings indicate a significant effect of seasonality on a range of human traits and that early-life seasons appear to have an effect on health and behaviors in adulthood.

1 | INTRODUCTION

Photoperiodic animals have evolved to mate seasonally to optimize their survival with environmental factors such as nutrients, temperature, sunlight, or predators being primary drivers. The circannual rhythms of organisms anticipate these natural conditions and prepare by regulating metabolism, energy storage and reproduction (Wood & Loudon, 2014). Humans are no longer influenced to the same extent by seasonal environmental drivers, although vestigial behaviors can still be observed in some nonindustrialized societies where conception rates are in line with food availability (Leslie & Fry, 1989). Socio-cultural components and small effect sizes make it difficult to detect the influence of seasonality (Foster & Roenneberg, 2008). The use of large sample sizes may contribute toward overcoming these issues. UK Biobank is a ~500 000 sample size adult community cohort study with detailed phenotype data. This cohort has already been used to show that low mood, anhedonia, body mass

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index (BMI), fat percentage, blood pressure, inflammation, and mortality related to cardiovascular problems are seasonal, with most peaking during winter months(Lyall et al., 2018; Wyse et al., 2018). However, seasonality of birth rate, basal metabolic rate (BMR), subjective health, and sleep have not been analyzed before in the UK Biobank.

Early developmental programming prepares offspring for the environmental challenges they may face. Unfavorable seasonal conditions may influence maturation, later-life health and reproductive success (Lummaa, 2003). Season of birth has been associated with a number of health problems (Boland, Shahn, Madigan, Hripcsak, & Tatonetti, 2015). In studies using data from UK Biobank, birth weight, age of menarche, adulthood height and educational qualifications have been linked to birth season (Day, Forouhi, Ong, & Perry, 2015). In addition, it has been demonstrated using 550 brain scans that season of birth may influence brain structure (Pantazatos, 2014). With more than 20 000 brain images, the UK Biobank cohort may provide insight into this topic.

This report firstly investigated seasonality of these characteristics comprising birth rate, BMR, health, and sleep. Secondly, it investigated whether season of birth is associated with gray matter volume, BMR, health, and sleep.

2 | METHODS

The study uses the UK Biobank resource (application 41 877) that is comprised of 502 536 participants (mean age at initial testing 56.5 ± 8.1 years, range 37-73 years; 54.4% female) (Sudlow et al., 2015). Details of data fields used in this report can be found in Tables S1 and S2. Season of birth was categorized according to day length as either long night (October to March, 49.1%) or short night (April to September, 50.9%). Season of test groups was also generated using day length categories.

Seasonality of births was tested using the Rayleigh test of uniformity. Subjective health rating ("excellent" or "good" vs "fair" or "poor") were analyzed using Walter and Elwood's test of seasonality for season of test. BMR, reaction speed (mean time to correctly identify matching cards) and sleep variables (sleep duration, ease of getting up, daytime dozing, insomnia, napping, and chronotype) were compared between season of test groups using linear regression, adjusted for age and sex. Individuals who reported they undertook shift work (N = 22 154) were excluded from the analysis of sleep variables.

Comparative height during childhood ("shorter" or "average" vs "taller") and health (subjective health rating, hearing problems, diabetes, cancer, eye problems, stroke, heart attack, hypertension, allergy, asthma,

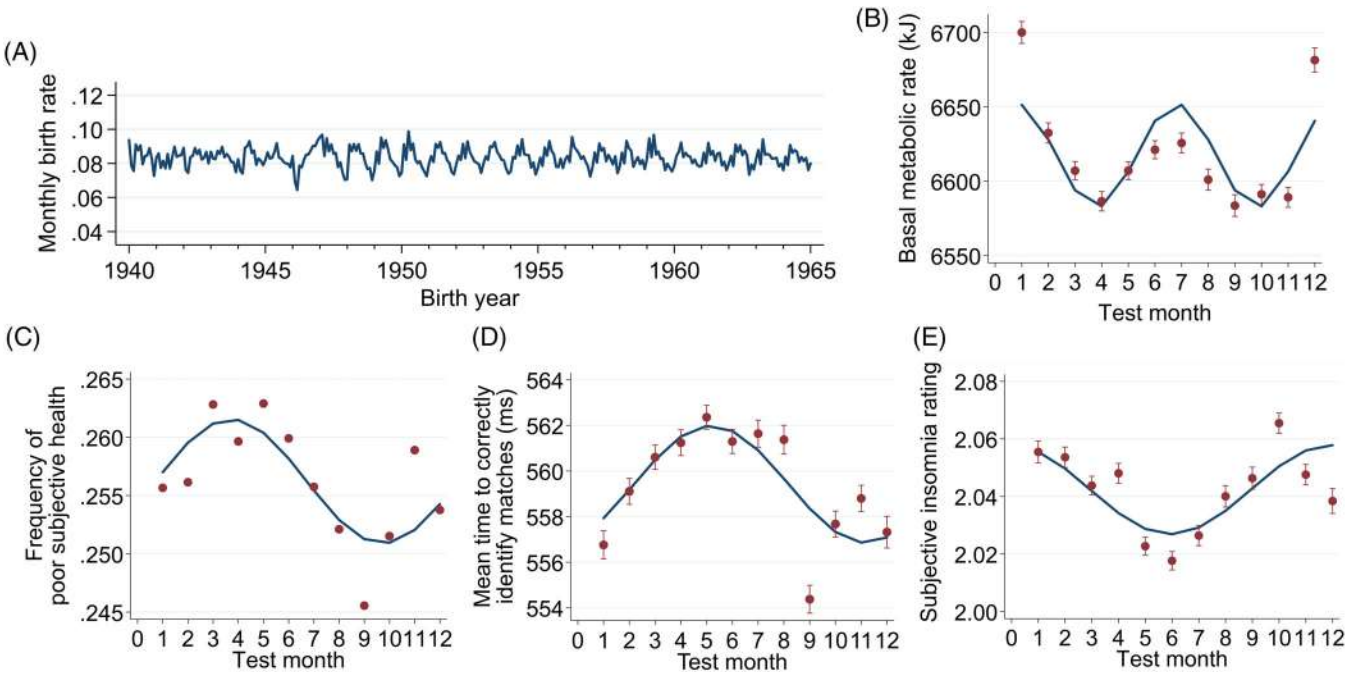

FIGURE 1 A, Monthly birth rate between 1940 and 1965 in the UK Biobank. B, Annual rhythm of basal metabolic rate. C) Annual rhythm of frequency of having poor subjective health ("In general how would you rate your overall health?" Excellent or good, fair or poor). D, Annual rhythm of reaction speed (mean time to correctly identify matches). E, Annual rhythm of subjective insomnia rating ("Do you have trouble falling asleep at night or do you wake up in the middle of the night?" 1 = never...3 = usually). In B, C, D, and E, blue line is trigonometric fit line. Red scatter plots show monthly prevalence in C and monthly mean ± standard error in B, D, and E

TABLE 1 Results of the statistical analyses for seasonality and season of birth effect of sleep variables, reaction time, and basal metabolic rate

	Age (years)	Gender (male)	Day length of test (short night)	Day length of birth (short night)
Basal metabolic rate (kJ/day)	$\beta = -18.908$	$\beta = 2132.849$	$\beta = 23.661$	$\beta = 10.880$
	SE = 0.149	SE = 2.425	SE = 2.422	SE = 2.415
	$P < .001$	$P < .001$	$P < .001$	$P < .001$
Reaction time (milliseconds)	$\beta = 4.001$	$\beta = -18.064$	$\beta = 1.786$	$\beta = -1.094$
	SE = 0.020	SE = 0.323	SE = 0.322	SE = 0.321
	$P < .001$	$P < .001$	$P < .001$	$P = .001$
Sleep duration (hours)	$\beta = 0.007$	$\beta = -0.036$	$\beta = -0.020$	$\beta = -0.005$
	SE < 0.001	SE = 0.003	SE = 0.003	SE = 0.003
	$P < .001$	$P < .001$	$P < .001$	$P = .116$
Napping (1 = never/rarely ... 3 = usually)	$\beta = 0.012$	$\beta = 0.142$	$\beta = 0.024$	$\beta < 0.001$
	SE < 0.001	SE = 0.002	SE = 0.002	SE = 0.002
	$P < .001$	$P < .001$	$P < .001$	$P = .784$
Insomnia (1 = never/rarely ... 3 = usually)	$\beta = 0.009$	$\beta = -0.203$	$\beta = -0.023$	$\beta = 0.011$
	SE < 0.001	SE = 0.002	SE = 0.002	SE = 0.002
	$P < .001$	$P < .001$	$P < .001$	$P < .001$
Daytime dozing (1 = never/rarely ... 4 = all of the time)	$\beta = 0.007$	$\beta = 0.036$	$\beta = 0.015$	$B < -0.001$
	SE < 0.001	SE = 0.001	SE = 0.001	SE = 0.001
	$P < .001$	$P < .001$	$P < .001$	$P = .999$
Chronotype (1 = definitely morning ... 4 = definitely evening)	$\beta = -0.011$	$\beta = 0.033$	$\beta = -0.016$	$\beta = -0.003$
	SE < 0.001	SE = 0.003	SE = 0.003	SE = 0.003
	$P < .001$	$P < .001$	$P < .001$	$P = .227$
Ease of getting up (1 = not at all ... 4 = very easy)	$\beta = 0.019$	$\beta = 0.186$	$\beta = 0.036$	$\beta = -0.007$
	SE < 0.001	SE = 0.002	SE = 0.002	SE = 0.002
	$P < .001$	$P < .001$	$P < .001$	$P = .001$

Note: Basal metabolic rate linear regression model: F(4, 492383)>99999, $P < .0001$, $R = .6145$; Reaction time linear regression model: F(4, 496704) = 10816.26, $P < .0001$, $R = .0801$; Sleep duration linear regression model: F(4, 476378) = 375.67, $P < .0001$, $R = .0031$; Napping linear regression model: F(4, 478594) = 5115.68, $P < .0001$, $R = .0410$; Insomnia linear regression model: F(4, 478938) = 3666.53, $P < .0001$, $R = .0297$; Daytime dozing linear regression model: F(4, 476862) = 1736.33, $P < .0001$, $R = .0144$; Chronotype linear regression model: F(4, 424978) = 914.82, $P < .0001$, $R = .0085$; Ease of getting up linear regression model: F(4, 475023) = 7013.23, $P < .0001$, $R = .0558$.
Abbreviations: β = Regression coefficient, SE = Standard error, P = P-value.

bronchitis, bipolar disorders, depression and having two or more health issues [multimorbidity]) were analyzed for season of birth effect using Walter and Elwood's test of seasonality. BMR, reaction speed, and sleep variables were compared between seasons of birth groups using linear regression, adjusted for age and sex. Associations between regional gray matter volumes (derived from T1 weighted images of structural brain MRI scans) and season of birth were analyzed using linear regression, adjusted for age, sex, and head size.

Bonferroni correction for multiple testing was applied and a P-value below 2×10^{-3} was accepted as significant for health and behavior outcomes. For brain image analysis, the P-value threshold was 3×10^{-4}. When a seasonal pattern or day length group differences had been detected, the data were graphed. To observe monthly distributions, trigonometric fit lines (unimodal or bimodal) were produced for each graph and monthly means or frequencies of variables were compared using one-way ANOVA with the Bonferroni post hoc test. Statistical analyses were performed using STATA (Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) and R (Agostinelli & Lund, 2017; Barnett, Baker & Dobson, 2018).

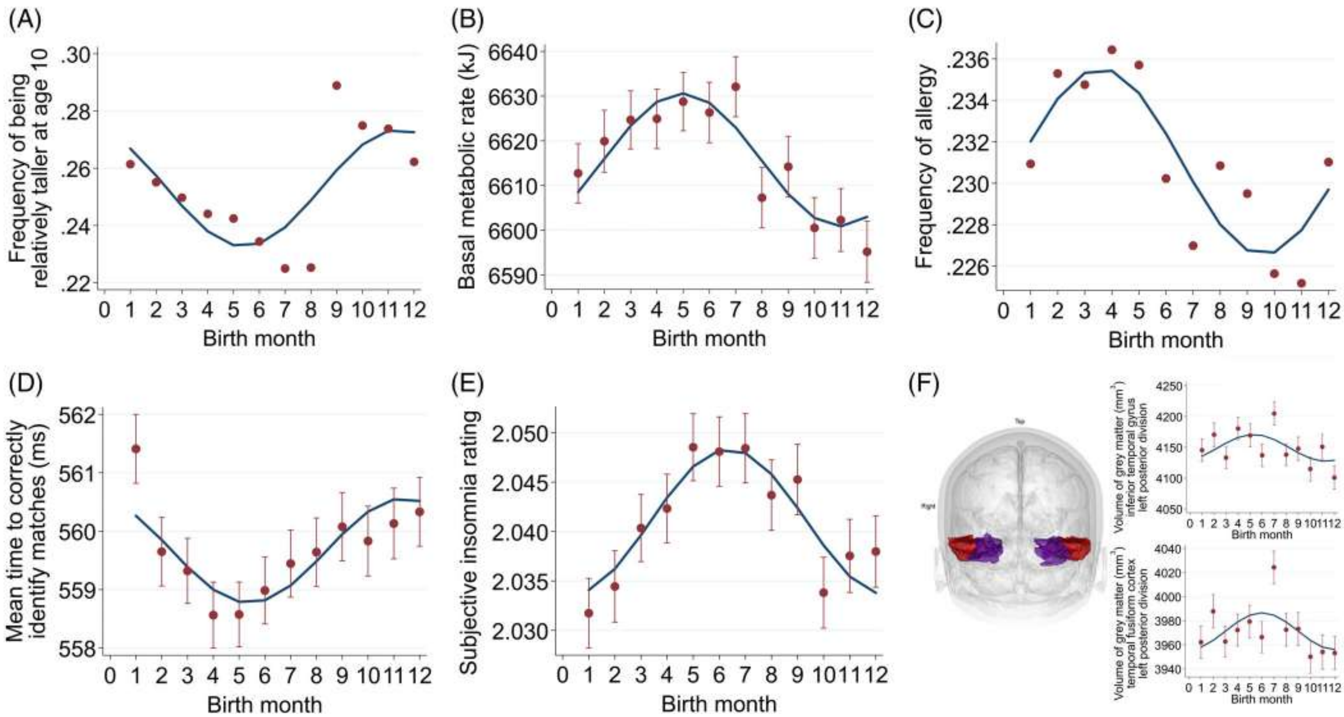

FIGURE 2 A, Month of birth and frequency of being taller at age 10 ("When you were 10 years old, compared to average would you describe yourself as"; taller, shorter or about average). B, Month of birth and basal metabolic rate. C, Month of birth and frequency of having allergy ("Has a doctor ever told you that you have had any of the following conditions?" Hayfever, allergic rhinitis or eczema). D, Month of birth and mean time to correctly identify matches. E, Month of birth and subjective insomnia rating ("Do you have trouble falling asleep at night or do you wake up in the middle of the night?" 1 = never...3 = usually). F, Representation of the two brain regions that had the lowest *P*-values. Purple color shows the temporal fusiform cortex and red color shows inferior temporal cortex. The top graph shows month of birth and volume of gray matter of inferior temporal gyrus, left posterior division. The bottom graph shows volume of gray matter of temporal fusiform cortex, left posterior division. Blue line is trigonometric fit line in all graphs. Red scatter plots show prevalence in A and C and mean ± standard error in B, D, E, and F

3 | RESULTS

3.1 | Influence of seasonal variation on UK Biobank phenotypes

We observed that birth rate is seasonal (Rayleigh statistics = 0.03, $P < .001$) with the majority of the births occurring between April and May (Figure 1A) and that seasonality existed for resting metabolic rate, health, reaction speed, and sleep (Table 1). Basal metabolism required higher daily energy in January compared with September (mean difference = −116.4 kJ, $P < .001$) with monthly distribution indicating a bimodal seasonality that has the lowest value during equinox months (Figure 1B). During autumn, individuals less frequently reported fair or poor health than in spring (May vs September mean difference = 1.7%, $P < .001$) (Figure 1C). A similar pattern was observed for reaction speed, where measurements recorded in May were slower than those in September (mean difference = −8.0 ms, $P < .001$) (Figure 1D). All sleep variables showed seasonality (Table 1). In June and July compared with winter months, people tended to sleep for shorter periods, went to sleep earlier, found it easier to get up and reported more daytime dozing and napping (Figure 1D). Insomnia peaked in autumn and winter and had nadir at spring and summer (June vs October mean difference = 0.048, $P < .001$) (Figure 1E).

3.2 | Influence of season of birth on UK Biobank phenotypes

People born in September compared to July (mean difference = 6.4%, $P < .001$) reported that they were relatively taller than their peers at age 10 (Figure 2A). BMR, allergy, reaction speed, and sleep variables were associated with season of birth. If people were born in July they had a higher BMR compared to people born in December (mean difference = −37.8 kJ, $P = .005$) (Figure 2B). Prevalence of allergy was the highest among those who were born in spring months (April vs November mean difference = 1.1%, $P = .010$) (Table S3, Figure 2C). Reaction time was faster in spring-born individuals than winter-born people (May vs January mean difference = 2.8 ms, $P = .034$) (Figure 2D). Season of birth effect was observed in insomnia and ease of getting up (Table 1). Spring and summer seasons of birth were associated with a higher insomnia rate compared with autumn and winter seasons of birth (May vs January mean difference = −0.017, $P = .039$) (Figure 2E). Cortical gray matter volumes were compared against day length groups (Table S4). None of the brain regions were significantly associated with season of birth after Bonferroni correction for multiple testing. However, posterior temporal fusiform cortex (B = 23.20, SE = 8.17, $P = .0045$) and posterior inferior temporal gyrus (B = 34.01, SE = 12.05, $P = .0048$) had the strongest association before correction, with the largest volumes associated with those born in July (Figure 2F).

4 | DISCUSSION

This report uses a large cohort study to provide evidence that seasonality can influence human reproduction, metabolism, sleep, and health. Unlike other animals, there is no universal human mating season as is associated with environmental conditions, food harvest and cultural beliefs (Foster & Roenneberg, 2008). However, similar to our results, late spring peak of birth rate has been observed in European countries (Foster & Roenneberg, 2008; Rojansky, Brzezinski, & Schenker, 1992). A previous study reported greater winter BMR compared to summer (Leonard et al., 2014). We showed daily energy demand has the highest value in winter and a second peak in summer. This bimodality may be due to increased weight and fat metabolism during winter and need of thermoregulation in both winter and summer.

The main seasonal cue is changing day length, which may alter circadian rhythms and sleep (Stothard et al., 2017). We have demonstrated that sleep characteristics are seasonal. It was previously shown that human brain activity responds differently to cognitive tests in different seasons (Meyer et al., 2016). We found that people have high attention with faster reaction speed in autumn compared to spring. A previous study showed an association between slow reaction time and mortality (Hagger-Johnson, Deary, Davies, Weiss, & Batty, 2014). In line with this, we found that autumn is the period when people are more likely to report good subjective health. These findings are important because they suggest that studies of sleep, cognition, and health should adjust for seasonal effects. They may also suggest that learning may be optimal for students at certain times of the year and that the use of increased lighting strength during dark months may help sleep disorders.

Consistent with the previous findings(Didikoglu, Maharani, Payton, Pendleton, & Canal, 2019; Stothard et al., 2017; Willetts, Hollowell, Aslett, Holmes, & Doherty, 2018), it was observed that late sleep timing and long sleep time are associated with longer periods of night darkness. Coherently, we found that people wake up more easily when the sun rises earlier. Low mood and anhedonia have been previously found to be higher in winter (Lyall et al., 2018) and we showed that insomnia has a similar pattern. Metabolic traits such as waist circumference, fat percentage, blood pressure, and BMI peak between January and March (Wyse et al., 2018) and we have shown that BMR accompanies these traits. We also showed that people generally rate themselves as having poor health in spring, after the peak period of metabolic traits. We showed that late spring and early summer is the peak period for slow reaction speed, more napping and daytime sleeping. (General seasonality pattern of the UK Biobank phenotypes can be seen in Figure S2).

We have also shown that season of birth may program later-life characteristics of humans. It has been reported that summer-born infants had a higher birth weight and spring-born females had an average age at menarche, compared to those born in summer (delayed puberty) and those born in autumn-winter (early puberty) (Day et al., 2015). These findings are consistent with our birth rate results and may show that late spring is a favorable birth period. We found that children born in autumn, when birth rate is close to the nadir, are generally taller than average. This may indicate that seasonal programming is a compensatory mechanism. Reaction speed was slower in spring but spring season of birth was associated with faster reaction speed. BMR was higher in winter but winter season of birth was associated with lower BMR. Insomnia was more frequent in autumn-winter but autumn-winter season of birth was associated with less frequent insomnia. Previous research suggested that seasonal programming may influence brain development and reported that structure of the superior temporal gyrus was associated with season of birth (Pantazatos, 2014). We observed a suggestive season of birth effect in structurally proximal regions, temporal fusiform cortex and inferior temporal gyrus but we could not replicate the superior temporal gyrus association. In addition, many diseases have been related to birth month (Boland et al., 2015). In our population, we observed an increase of allergy among spring-born participants. Association between season of birth and allergy has been explained as sensitization to allergens like home dust mites or pollens in early-life (Boland et al., 2015).

There are some limitations in this study. Day length of birth groups were generated using month of birth instead of the exact birthday due to privacy of participants' birthdays that were not obtained. All health and behavioral data in this study were self-reported. The seasonality and season of birth effects may be valid for only a British population or those living in similar latitudes. In addition, this study only investigated cross-sectional data. A longitudinal study may help us to better understand within-individual seasonal patterns.

The shift from hunter-gatherers to modern society has reduced our interaction with natural seasonal cues. Despite this, it is possible to detect an annual rhythm from birth to death. Our study provides further evidence of seasonality and season of birth influence on later-life behavior and health. These results support previous findings and add to the growing evidence that seasonality may be important and should be taken into account when conducting population health studies.

ACKNOWLEDGMENTS

A. D. was supported by a grant from the Republic of Turkey Ministry of National Education.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Altug Didikoglu, Maria Mercè Canal, Antony Payton, and Neil Pendleton designed the study. Altug Didikoglu wrote the manuscript and performed the statistical analysis. Antony Payton, Maria Mercè Canal, and Neil Pendleton supervised the project. All authors contributed to the writing and have approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Didikoglu A, Canal MM, Pendleton N, Payton A. Seasonality and season of birth effect in the UK Biobank cohort. *Am J Hum Biol*. 2020;e23417. https://doi.org/10.1002/ajhb.23417