Is Heart Rate Variability Related to Season of Birth?

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ABSTRACT

Background: Season of birth (SOB) has been found to be related to cardiovascular mortality, but the mechanisms are unclear. It is suggested that birth in winter is a protective factor for the circulatory system, and this should be able to be observed using heart rate variability (HRV) measurements. The phenomenon may have a sex difference and is likely to be modulated by climatic factors. This study focused on this problem and investigates healthy school-age children to minimize confounding factors.

Hypothesis: Birth in winter is protective to cardiovascular system via autonomic modulation. There is a gender difference in the relationship between SOB and autonomic activity. Climatic factors are the cause of SOB effects on autonomic system.

Methods: A total of 381 healthy school-age children were recruited for this study. Their HRV profiles were measured once and climatic information related to their month of birth was gathered. The HRV profiles of the 2 sexes and 4 seasons of birth were compared. Correlation and regression analysis were performed to clarify the relationship between climatic factors and the HRV results.

Results: Boys born in winter have higher high-frequency power (HF) but a lower ratio of low-frequency power to high-frequency power (LF/HF) than do males born in other seasons. This result is not found for girls. Age and the temperature of the SOB are predictive factors for HF among boys. The humidity of SOB is a predictive factor for normalized low-frequency power (LF%) and LF/HF among girls.

Conclusions: Season of birth is related to both parasympathetic and sympathetic activity among school-age children, especially boys. Temperature and humidity are potential causes of this SOB phenomenon.

Introduction

Season of birth (SOB) has been found to be related to many physical and psychiatric disorders, such as epilepsy, Parkinsonism, schizophrenia, dementia, autism, and Down syndrome.^{1–6} However, there has been no conclusive findings concerning the influence of SOB on the cardiovascular system. A meaningful relationship between birth in spring and low blood pressure among men has also

been reported, although the sample size was relatively low.⁷ Another epidemiological study revealed that cardiovascular mortality differs according to the month of birth.⁸ In Germany, the average age for cardiovascular death is the lowest with a May birth and highest with a November birth; the trends for the 2 sexes are similar, but the trend for men is more significant than for women.⁸ These studies provide new insights into the effect of SOB on the circulatory system; however, the mechanisms remain unclear.

The phenomenon of SOB implies that environmental factors during the prenatal and postnatal period may have a persistent effect on the subjects. Several factors have been listed as etiologies of the SOB phenomenon: climate, infection, nutrition, and prenatal stress.^{2,8–10} In terms of climate, the influences of temperature, sunlight, and humidity have been discussed.^{11–18} A Polish study shows that the birth length of boys is related to all of the above atmospheric factors.¹⁵ A temperature hypothesis

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for the development of schizophrenia has been put forward, although its effect may be indirect.² Both in humans and animals, circadian rhythm is influenced by the perinatal photoperiod, which is parallel to sunlight exposure.^{19,20} All of these climatic factors have been suggested as explanations for various types of physiological or psychological phenomena, including personality.²¹ However, a discussion on the effect of these factors on the circulatory system is still lacking. One possibility is that personality traits may act as a mediator between climate and cardiovascular risk.²²

Much research has indicated that autonomic activities have a significant role in cardiovascular risk. Up to the present, several methods have been developed to examine autonomic functioning, such as heart rate variability (HRV), baroreflex sensitivity, and pre-ejection period.^{23–26} Among them, HRV is a noninvasive and easily used tool. By gathering 5 minutes of heart rate signals and switching to frequency domain data, sympathetic and parasympathetic activities can be clearly distinguished. Research evidence supports HRV indexes as good predictive factors for cardiovascular risk.^{27–29} Thus, we believe that HRV measurement is able to provide information that will aid our understanding of the effect of SOB on cardiovascular mortality.

Heart rate variability is a sensitive evaluating tool, and its results can be affected by the presence of biological disease, the individual's psychological state, and the use of medication.^{30–34} Therefore, among subjects with complicated physical and psychiatric conditions, such as the elderly, there are many confounding factors that need to be considered. In addition, if the duration between the age of measurement and birth age is longer, more events will have affected the HRV. As a result of the above factors, we considered children to be the most suitable group for this investigation. Our previous research has revealed that HRV shows a sex difference and that this phenomenon also can be found in children.^{25,35,36} Whether this phenomenon is related to SOB is also an interesting topic.

We examine 3 hypotheses in this study. First, we hypothesize that birth in winter is a protective factor in relation to cardiovascular diseases and that this may be observed as a specific autonomic presentation. Second, we hypothesize that a sex difference is present in the relationship between SOB and autonomic activity. Third, we hypothesize that various climatic factors, such as temperature, humidity, and sunlight, are contributing factors to the effects of SOB. Based on the above hypotheses, we designed a cross-sectional study. To minimize potential confounding factors, the targets of this research were healthy school-age children.

Methods

Study Sample

We evaluated 382 subjects (205 males and 177 females), age 6 to 10 years, from elementary schools in Taipei. Cluster sampling method was adopted for subject selection. Subjects with diseases that might affect the HRV results (cardiovascular disease, cancer, neuropathy, and psychiatric disorders) were excluded. Subjects who were using medication that has been reported to affect cardiovascular fluctuations (such as

hypnotics, autonomic blockers, known substance abuse, psychoactive drugs, or neuroleptic medications) were also excluded. Informed written consent was obtained from all participants and their parents, and the experiment protocol was approved by the Ethics Committee of Department of Education and Research, Taipei City Hospital, Taipei.

Experiment Design

All subjects were enrolled in this study between April 2011 and October 2011. The weight, height, and age of the subjects were recorded. The body mass index (BMI) of each subject was calculated for further analysis. Age and BMI were regularly recorded because their influence on HRV has been reported in previous studies.^{21,25,37} All subjects were asked to rest for 5 to 10 minutes before recording. A lead I electrocardiogram (ECG) was then taken for 5 minutes while each subject sat quietly and breathed normally over the 5-minute period. All subjects were asked to keep from falling asleep. The recording was performed in the daytime to reduce the possible diurnal change of HRV.

Heart Rate Variability

The procedure for 5-minute HRV analysis was based on the standard method and has been described previously.^{24,25} An HRV analyzer (SS1C; Enjoy Research Inc., Hualien, Taiwan) was used for acquisition, storage, and processing of ECG signals. Signals were recorded by an 8-bit analog-to-digital converter with a sampling rate of 512 Hz. The digitized ECG signals were analyzed immediately and simultaneously stored for further verification. According to likelihood using a standard QRS template, the computer algorithm identified each QRS complex and rejected each abnormal signal (such as ventricular premature complex or noise). Stationary R-R interval values were resampled and interpolated at a rate of 7.11 Hz for producing continuity in the time domain. This interpolation produced 2048 data points over 288 seconds. Via Fourier transformation, the power spectrum was then quantified into the frequency-domain measurements, which were defined previously.^{24,25} The frequency domain indexes included total power (TP), very low-frequency power (VLF; 0.003–0.04 Hz), low-frequency power (LF; 0.04–0.15 Hz), high-frequency power (HF; 0.15–0.40 Hz), LF/HF, and normalized LF (LF%). LF% was defined as $LF/(TP - VLF) \times 100$. For correcting the skewed distributions, TP, VLF, LF, HF, and LF/HF were logarithmically transformed.²⁵ HF is a parasympathetic index, whereas LF% and LF/HF represent sympathetic function.^{24,25}

Climatic Data

We obtained the daily meteorological data (temperature, humidity, and sunshine) from the Central Weather Bureau, Taiwan. The dataset was divided into 4 seasons: spring (March to May), summer (June to August), fall (September to November), and winter (December to February).

Statistical Analysis

The parameters among the 4 seasons were compared by analysis of variance (ANOVA). The Bonferroni method was adopted for the post-hoc analysis. The relationships between

Table 1. Comparison of the HRV Parameters Across Children Born in 4 Seasons

Boys	Spring (n = 46)	Summer (n = 44)	Fall (n = 67)	Winter (n = 48)	F Test (ANOVA)	P Value	Comparison
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
Age, y	9.27 (1.68)	9.15 (1.63)	9.67 (1.56)	9.80 (1.68)	1.788	0.151	—
BMI, kg/m ²	19.88 (4.53)	18.85 (3.75)	18.65 (3.20)	18.74 (4.05)	1.08	0.358	—
RR, msec	639.96 (83.18)	628.14 (84.18)	624.54 (69.21)	647.85 (68.19)	0.995	0.396	—
TP, ln(ms ²)	7.52 (0.91)	7.57 (0.93)	7.48 (0.70)	7.89 (0.74)	2.558	0.056	—
HF, ln(ms ²)	5.53 (1.15)	5.57 (1.06)	5.48 (0.87)	6.15 (1.04)	4.813	0.003 ^a	Winter > spring, summer, fall
LF, ln(ms ²)	6.33 (1.02)	6.55 (0.95)	6.43 (0.83)	6.80 (0.73)	2.641	0.051	—
VLF, ln(ms ²)	7.52 (0.91)	7.57 (0.93)	7.48 (0.70)	7.88 (0.74)	2.552	0.057	—
LF/HF [ln(ratio)]	0.80 (0.62)	0.98 (0.67)	0.95 (0.55)	0.65 (0.63)	3.02	0.031 ^a	Summer, fall > winter
LF%, nu	58.47 (12.26)	61.90 (14.33)	61.48 (12.23)	56.03 (13.93)	2.213	0.088	—
Girls	Spring (n = 34)	Summer (n = 41)	Fall (n = 57)	Winter (n = 45)	F Test	P Value	Comparison
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)			
Age, y	9.64 (1.55)	9.23 (1.76)	9.45 (1.60)	8.92 (1.64)	1.475	0.223	—
BMI, kg/m ²	17.44 (3.35)	17.51 (3.28)	16.94 (3.08)	18.18 (3.32)	1.234	0.299	—
RR, msec	639.91 (87.21)	643.46 (73.58)	628.09 (70.96)	633.40 (62.88)	0.367	0.777	—
TP, ln(ms ²)	7.69 (0.89)	7.84 (0.65)	7.57 (0.76)	7.53 (0.79)	1.401	0.244	—
HF, ln(ms ²)	5.86 (1.08)	6.07 (0.85)	5.62 (1.08)	5.68 (1.01)	1.775	0.154	—
LF, ln(ms ²)	6.68 (0.87)	6.66 (0.70)	6.43 (0.85)	6.41 (0.73)	1.423	0.238	—
VLF, ln(ms ²)	7.69 (0.89)	7.83 (0.65)	7.56 (0.76)	7.53 (0.79)	1.399	0.245	—
LF/HF [ln(ratio)]	0.82 (0.56)	0.60 (0.51)	0.81 (0.65)	0.74 (0.62)	1.239	0.297	—
LF%, nu	60.42 (13.03)	53.53 (10.99)	58.70 (13.23)	56.71 (13.03)	2.169	0.093	—

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; HF, high-frequency power of HRV; HRV, heart rate variability; LF, low-frequency power of HRV; LF%, normalized LF; LF/HF, LF to HF ratio; nu, normalized unit; RR, R-R interval values; SD, standard deviation; TP, total power of HRV; VLF, very low-frequency power of HRV.

^aP < 0.05 between 4 seasons by ANOVA.

HRV and demographic/climatic factors that are likely to affect HRV were analyzed using correlation and multiple linear regression analysis.

Results

The results were divided into 2 groups, one for males and the other for females. Demographic data for the boys and girls showed that there was no significant difference in age or BMI across the 4 seasons (Table 1). A comparison of HRV parameters reveals that there are significant differences for HF and LF/HF among the 4 seasons among boys. Boys born in winter have significantly higher HF than those born in the other 3 seasons. Boys born in summer and fall have a significantly higher LF/HF than those born in winter (Figure 1). The TP, LF, and LF% of boys do not reveal any significant difference across the 4 seasons. With regard to girls, the HRV parameters show no significant difference across the 4 seasons (Table 1).

The correlations between HRV parameters and demographic/climatic factors among boys showed significantly positive correlations for the following pairs: age-TP ($r = 0.204$), age-HF ($r = 0.159$), and age-LF ($r = 0.222$). However, this was not true for age-LF/HF and age-LF%. Among girls, age was found to be positively correlated with TP ($r = 0.204$), LF ($r = 0.154$), and LF% ($r = 0.148$). There was no significant correlation between any HRV parameters and BMI for either sex. It is interesting to note that the temperature at birth was found to be negatively correlated with HF ($r = -0.161$) among boys, whereas the humidity at birth was found to be negatively correlated with LF/HF ($r = -0.148$) and LF% ($r = -0.168$) among girls. Sunshine at birth did not show any meaningful correlation with the HRV parameters of either sex (Table 2).

Multiple linear regression analysis reveals that age and temperature at birth were predictive of HF among boys, whereas humidity at birth was a predictive factor of LF/HF

Figure 1. The values in HF and LF to HF ratio (LF/HF) of HRV among boys and girls born in different seasons. Values are means $\pm$ SEM. * $P < 0.05$ from vs winter. Abbreviations: HF, high-frequency power; HRV, heart rate variability; LF, low-frequency power; ln, natural logarithm; SEM, standard error of the mean.

Table 2. Correlations Between HRV Parameters and Demographic/Climatic Factors

	TP, ln(ms ²)	HF, ln(ms ²)	LF, ln(ms ²)	LF/HF, ln(ratio)	LF%, nu
Boys					
Age, y	0.204 ^a	0.159 ^a	0.222 ^a	0.05	0.095
BMI, kg/m ²	−0.072	−0.018	−0.07	−0.071	−0.025
Temperature, °C	−0.105	−0.161 ^a	−0.096	0.133	0.108
Humidity, %	−0.017	0.029	0.018	−0.022	−0.014
Sunshine, h/mo	−0.076	−0.098	−0.108	0.01	−0.008
Girls					
Age, y	0.204 ^a	0.061	0.154 ^a	0.1	0.148 ^a
BMI, kg/m ²	0.03	0.044	−0.019	−0.101	−0.092
Temperature, °C	0.119	0.095	0.083	−0.052	−0.061
Humidity, %	−0.061	−0.113	−0.034	−0.148 ^a	−0.168 ^a
Sunshine, h/mo	0.048	0.066	0.028	−0.075	−0.125

Abbreviations: BMI, body mass index; HF, high-frequency power of HRV; HRV, heart rate variability; LF, low-frequency power of HRV; LF%, normalized LF; LF/HF, LF to HF ratio of HRV; nu, normalized unit; TP, total power of HRV.
^a $P < 0.05$ by Pearson correlation analysis.

and LF% among girls. Age was found to have no significant meaning with respect to the regression model among girls (Table 3).

Discussion

There are 3 major findings in this study. First, comparing the HRV profiles across the 4 seasons, boys born in winter have a higher HF and a lower LF/HF than those who are born in other seasons. Second, no significant HRV difference

Table 3. Predictive Factors for HRV Parameters Using Multiple Regression Analysis

Boys	HF, ln(ms ²) $R^2 = 0.048$	
	β	P Value
Age, y	0.148	0.033 ^a
Temperature, °C	−0.149	0.031 ^a
Girls	LF/HF, ln(ratio) $R^2 = 0.022$	
	β	P Value
Age, y	0.062	0.425
Humidity, %	−0.148	0.049 ^a
Boys	LF%, nu $R^2 = 0.028$	
	β	P Value
Age, y	0.062	0.425
Humidity, %	−0.148	0.049 ^a

Abbreviations: HF, high-frequency power of HRV; HRV, heart rate variability; LF, low-frequency power of HRV; LF%, normalized LF; LF/HF, LF to HF ratio of HRV; nu, normalized unit.
^a $P < 0.05$ by simple linear regression analysis.

was found to be present for girls born across the 4 seasons. This is compatible with our hypothesis of a sex difference. Third, the results of correlation and regression analysis reveal that the HF among boys is significantly correlated with age and temperature during the SOB, whereas LF% and LF/HF among girls is correlated with humidity during the SOB. These results support the hypothesis that climatic factors may be potential causes of the SOB phenomenon that affects HRV.

Boys born in winter have high parasympathetic and low sympathetic activity, which are protective factors for cardiovascular diseases. If we view “cardiovascular death occurred at a younger age” as “having higher cardiovascular risk,” our finding seems to be compatible with the study by Reffelmann et al.⁸ Their analysis does not point out the sex difference. But considering the difference of the death age in distinct SOB, the trend of male subjects is more obvious. Further analysis reveals that a low temperature during the SOB is a potential cause of the high vagal modulation. The influence of temperature on HRV may be a direct or an indirect phenomenon. In terms of a direct effect, we assume that a low temperature during the postnatal period is a stress on the newborns. To balance the stress, the parasympathetic system may be enhanced, and this ability is then preserved into later life. Though there is not yet evidence finding a persistent physiological impact after suffering low temperature during childhood, several studies have indicated the presence of an ambient temperature effect on HRV among adults.^{37–39} The predominance of parasympathetic activity during stage-2 sleep is related to low temperature.³⁸ However, other research has shown that a low room temperature is a contributing factor toward enhanced sympathetic modulation.³⁷ Therefore, the effect of low ambient temperature on the autonomic system is inconsistent, and we wonder whether the influence of temperature on newborns and adults may be different. On the other hand, any indirect effect should involve modulation via the brain. Season of birth has been shown to be related to many psychiatric and neurological disorders, and there has been abundant research focusing on the mechanisms

by which these effects occur within the central nervous system. It has been found that subjects born in winter have high homovanillic acid and 5-hydroxyindoleacetic acid in their cerebrospinal fluid.⁴⁰ Homovanillic acid and 5-hydroxyindoleacetic acid are metabolites of dopamine and serotonin, respectively. Therefore, this implies that birth in winter is related to high dopamine and serotonin activity in the brain. Depressive disorders and anxiety disorders are generally considered to be caused by serotonergic hypoactivity.^{41–43} Anxiety is usually negatively correlated with parasympathetic modulation but positively correlated with sympathetic modulation.^{31,44,45} The findings are compatible with our results for boys born in winter. The relation among HF and LF/HF of boys born in winter, their serotonin activity, and levels of anxiety warrants further exploration.

Females born across the 4 seasons do not show significant differences in their HRV data. Such a sex difference has also been found during some other HRV studies.^{31,36} Several hypotheses have been put forward to explain this feature, such as parasympathetic dominance in females, different activity level in the 2 genders, and the impact of hormones.^{31,36} Some female subjects in our study were age >11 and thus may have been entering puberty. Therefore, the influence of sex-hormone levels cannot be totally ruled out. From another point of view, regression analysis disclosed that humidity during the SOB is a predictive factor with respect to 2 sympathetic indices, LF% and LF/HF. Past studies have indicated that humidity may affect the amount of water loss in newborns, which is in turn related to thermoregulation.¹⁴ Water balance is also highly related to orthostatic tolerance.⁴⁶ We wonder whether these effects may have knock-on effects on autonomic and circulatory functioning and that females may be more sensitive to potential water loss than males.

Another interesting finding is the positive correlation between HRV power and age in our study sample. The relation between age and HF in boys is especially significant. Studies focused on adults show that aging is associated with decreased HRV power,²⁵ but the effect on children is not identical. Several researchers disclose that HF and standard deviation of normal to normal intervals of R-R intervals (SDNN) increases with age during childhood^{47,48}; other studies show opposite results.^{49,50} In our opinion, during adulthood, the function of the autonomic nervous system may slowly decrease with age; but in a younger population, because the maturity of the autonomic nervous system does not reach its peak, HRV may transiently increase with age. The assumption awaits further investigation.

Study Limitations

Though the results are compatible with our 3 hypotheses, several limitations of this research should be discussed. The sample size of our study is relatively low, and the relationship between autonomic findings and birth during winter needs a higher population to confirm these relationships. In addition, Taiwan is in subtropical area, and climatic effects in other areas of the world may be quite different. The climatic data of the 4 seasons in Taiwan during SOB of subjects are shown in Table 4. The 4 seasons in Taiwan and in Europe

Table 4. Climatic Data of the 4 Seasons in Taiwan During SOB of Subjects

	Spring	Summer	Fall	Winter
Temperature, °C	22.57 (2.54)	28.82 (1.03)	24.85 (2.48)	17.37 (1.08)
Humidity, %	77.22 (3.65)	75.54 (3.34)	76.17 (3.92)	77.14 (3.02)
Sunshine, h/mo	100.20 (31.13)	159.23 (39.39)	110.08 (43.07)	87.14 (38.64)
Atmospheric pressure, Pa	1011.98 (2.64)	1005.40 (1.38)	1012.59 (3.82)	1019.73 (1.52)
Abbreviations: SD, standard deviation; SOB, season of birth. Data are presented as mean (SD).				

are distinctly different, and therefore any SOB phenomena should be interpreted carefully in the light of this. The months during which the HRV measurements took place were from April to October; whether this might have had any influence on the results is unclear. Although subjects with physical illness were excluded, various other factors (such as emotions and/or physical activities) that may interfere with HRV profiles were not recorded or corrected in this study. Long-term HRV measurement (for example, with duration of 24 hours) may be helpful for reducing the influence of confounding factors. Finally, the features of HRV are not identical to those of cardiovascular disease, despite autonomic imbalance being an important risk factor for them.

Conclusion

This study provides a possible explanation for relationships between SOB and the circulatory system. Autonomic activity is an observable target when exploring such phenomena, and the effect of SOB on the 2 sexes needs to be explored separately. Compared with the epidemiological findings presented in the past, the identification of a potential autonomic mechanism is an evolutionary step forward in the study of this area. Nevertheless, whether the influence of atmospheric factors on HRV is direct still needs to be investigated. We also expect that this topic will be explored using different age groups and in a variety of geographical areas with distinct climates.

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