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Original Article

Night-time cardiac autonomic modulation as a function of sleep–wake stages is modified in otherwise healthy overweight adolescents

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ABSTRACT

Objective: Even though sympathetic dominance during the daytime period is well known, currently, scarce data exist on autonomic nervous system (ANS) regulation during sleep in pediatric obesity. We aimed to evaluate sleep cardiac ANS regulation in normal-weight (NW) and overweight and obese (OW) adolescents.

Patients/methods: In this study, 60 healthy adolescents (15.7 ± 0.7 years) belonging to a birth cohort since infancy were classified based on body mass index percentiles criteria as: OW ($N = 27$) or NW ($N = 33$). Sleep was evaluated by polysomnography (PSG) during two consecutive in-lab overnight sessions. Non-rapid eye movement (non-REM) sleep stages (stages 1, 2, and slow-wave sleep [SWS]), rapid eye movement (REM) sleep, and wakefulness (Wake) were scored. R-waves were detected automatically in the electrocardiographic (ECG) signal. An all-night heart rate variability analysis was conducted in the ECG signal, with several time- and frequency-domain measures calculated for each sleep–wake stage. Sleep time was divided into thirds (T1, T2, T3). The analysis was performed using a mixed-effects linear regression model.

Results: Sleep organization was comparable except for reduced REM sleep percentage in the OW group ($p < 0.04$). Shorter R–R intervals were found for all sleep stages in the OW group; time-domain measured standard deviation of all R–R intervals (RRSD) was lower during stage 2, SWS and REM sleep (all $p < 0.05$). The square root of the mean of the sum of the squares of differences between adjacent R–R intervals (RMSSD) was also lower only during wake after sleep onset (WASO) in T1 and T3 ($p < 0.05$). The OW group had increased very low- and low-frequency (LF) power during WASO (in T1 and T2), and LF power during stage 2 and REM sleep (in T2). During WASO in the OW group, high-frequency (HF) power was lower (in T1 and T2), and LF/HF ratio was higher (in T2, $p < 0.007$).

Conclusions: Several sleep-stage-dependent changes in cardiac autonomic regulation characterized the OW group. As sleep-related ANS balance was disturbed in the absence of concomitant metabolic alterations in this sample of otherwise healthy OW adolescents, their relevance for pediatric obesity should be further explored throughout development.

1. Introduction

Childhood obesity and the proportion of overweight (OW) children has become an epidemic [1,2]. Moreover, childhood obesity is associated with several adverse health consequences

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including early onset of type 2 diabetes, dyslipidemia, high blood pressure, depressive symptomatology, and low self-esteem [1,3]. Unfortunately, common strategies for preventing or treating childhood obesity have shown moderate or only short-term effects [4].

Several factors such as sleep patterns may influence the development of pediatric OW and obesity [5,6]. Sleep is relevant for human well-being throughout the lifetime, and both short and disturbed sleep have been associated with metabolic dysfunction [7,8]. Autonomic nervous system (ANS) activity has also been implicated in the pathogenesis of obesity [9]. Continuous dynamic interaction between sympathetic and parasympathetic components establishes the ANS balance. The role of this balance on metabolic derangements has been studied in detail during wakefulness but to a markedly lesser extent during sleep [9,10]. Indeed, sleep has a relevant influence on ANS functioning [11], and sleep alterations can precede ANS disturbances.

Heart rate variability (HRV) is an accepted approach to estimate ANS tone. Sleep-state-dependent changes in HRV pattern are within the restorative processes that occur during sleep [12]. Sleep is divided into two states, rapid eye movement (REM) sleep and non-REM (non-REM) sleep [13]. Sleep state-related ANS tone includes a higher sympathetic tone and lower vagal tone in REM sleep relative to non-REM sleep [14]. Failure to achieve parasympathetic nervous system (PNS) dominance during sleep compared to the wake state has been associated with cardiovascular morbidity [15], and a persistent sympathetic dominance is associated with sleep disorders such as obstructive sleep apnea (OSA) [16], and periodic leg movements [17], and also with hypertension [18], type 2 diabetes [19], obesity [9] and cardiovascular diseases [10,20].

We and others have already reported alterations in sleep organization in OW children and adolescents, even in the absence of other apparent health problems or clinically evident sleep disorders [21–23]. Altered sleep-related HRV patterns – lower parasympathetic tone and higher sympathetic tone – could be early markers of ANS dysregulation in OW individuals [24]. Because most data on impaired ANS balance in pediatric obesity were obtained during the daytime wake or sleep time as a whole (without sleep stages differentiation), our aim was to compare ANS patterns as a function of sleep–wake states throughout the night-time between OW adolescents and normal-weight (NW) peers, all belonging to a birth cohort evaluated since infancy [25].

2. Material and methods

Studied adolescents were participants in an ongoing research in Chile on the behavioral, developmental, neurosensory, cognitive, and sleep–wake pattern effects of iron-deficiency anemia (IDA) in infancy. For this study, we included 65 healthy adolescents who had been evaluated neurophysiologically in the Sleep Laboratory, Institute of Nutrition and Food Technology (INTA), University of Chile. Detailed descriptions of the population, study design, and findings during infancy and childhood have been previously published [26,27]. Adolescents were free from acute or chronic illnesses, without sleep disorders (eg, restless legs syndrome or periodic leg movements syndrome), and with an apnea–hypopnea index (AHI) <5/h. Parents of adolescents below 18 years old provided signed informed consent (and their children gave assent), and adolescents above 18 years old provided signed informed consent. The original and follow-up research protocols were approved and reviewed in accordance with the Declaration of Helsinki by the Institutional Review Boards of the University of Michigan Medical Center, Ann Arbor, USA, and INTA, University of Chile, Santiago, Chile.

2.1. Polysomnographic evaluation

Each adolescent underwent two-consecutive all-night polysomnographic (PSG) recordings. The first served as an adaptation night; the second night was used for all sleep and HRV analyses. Because the procedures were carried out following the individual's routine time schedules, PSG recordings started at the subject's usual bedtime and continued until spontaneous awakening the next morning.

PSG included continuous monitoring of the following signals: electro-encephalogram with electrode placement according to the 10–20 system [28] (F3, F4, C3, C4, O1, O2) referenced to the contralateral mastoid. The settings included two electro-oculograms, chin electromyogram, left and right tibialis electromyogram, electrocardiogram (ECG), thermistor and nasal pressure cannula, thoracic and abdominal efforts, peripheral oxygen saturation, snoring and position sensors. PSG recordings were performed with a Cadwell Easy EEG II system (Cadwell Lab., Kennewick, WA, USA). After the acquisition, data were stored in digital format, and each PSG record was then transformed off-line to the European Data Format for further analysis [29].

2.2. Anthropometry assessment

Before each PSG assessment, measurements of weight and height were carried out with each adolescent wearing light clothes and no shoes using a Seca scale (Seca® 700, Hamburg, Germany). Weight was measured with an accuracy of 100 g and height was measured in a fixed tallimeter with an accuracy of 1 cm. Body mass index (BMI, weight (kg)/(height (m))^2) was calculated and classified according to age- and sex-BMI percentiles (BMIp) following the World Health Organization (WHO) charts for children and adolescents [30]. Participants were categorized into two groups: NW ($5 \leq$ BMIp $<$ 85th centile) or OW (BMIp $\geq$ 85th centile).

2.3. Sleep–wake stages scoring and processing

Sleep stages were scored in 30-s epochs defining non-REM sleep stages as S1, S2, and SWS, REM sleep and wakefulness (Wake), according to international standard criteria [31]. All sleep measures were processed without knowledge of whether a given child was NW or OW. Respiratory events during sleep were detected by semi-automated processing using Cadwell Easy EEG II software (Cadwell Lab., Kennewick, WA, USA) and scored if they lasted two or more respiratory cycles. Apnea and hypopnea were defined based on the American Academy of Sleep Medicine criteria [32]. After automated detection, visual editing of the whole recording was performed to add, confirm, or reject respiratory events, and a final score was obtained (number of respiratory events/h of total sleep time (TST)).

The following conventional sleep parameters were calculated using a method previously reported [33]:

Time in bed (TIB): elapsed time from lights-off to lights on in the room, in minutes;

Sleep period time (SPT): time from sleep onset to sleep end, in minutes;

TST: SPT minus time awake during SPT, in minutes;

Sleep latency: time from lights-out to sleep onset, defined as the first epoch of any sleep stage, in minutes;

REM sleep latency: time from sleep onset to the first REM sleep epoch, in minutes;

Sleep efficiency: the ratio between TST and SPT (TST/SPT*100), as a percentage;

Wake after sleep onset (WASO): including all Wake epochs during SPT;

Sleep cycle duration: time elapsed between the first epoch of any non-REM sleep stage to the last epoch of the succeeding REM sleep episode (of at least 1 min duration), in minutes;

Time spent in WASO: percentage of the SPT spent in Wake, as a percentage;

Time spent in each non-REM sleep stage and in REM sleep.

Sleep was also studied regarding the number, total time and mean duration of each sleep–wake stage episode. As previously reported by our group [21,26], and in order to achieve an analytic approach to temporal changes of HRV across the night, sleep and HRV data were analyzed for each third (thirds 1, 2 and 3) of SPT.

2.4. Electrocardiographic signal processing

All-night electrocardiographic (ECG) signal was processed offline using the software Hypnolab 1.2, SWS Soft, Italy (for details, see Ferri et al., [34]) which is fully compliant with standard recommendations [35]. ECG recordings (one derivation) were checked quality based on 5-min epochs, and one researcher visually checked the recording for potential artifacts and/or electrical noise before running the analyses. These epochs were individually chosen and did not contain periodic leg movements syndrome or gross body movements. During all epochs chosen for HRV analysis, patients rested in supine or lateral positions. Finally, the eventual presence of apneas and hypopneas was carefully controlled so that the epochs selected for analysis were free from potentially interfering respiratory events. For analysis, a mean of 35 5-min epochs was included for each corresponding third of the night. The results of the subsequent HRV analysis were averaged for each recording, for each sleep stage, in order to obtain a single series of values to be used for the statistical analysis of the results.

In each 5-min epoch, the ECG signal (sampled at least at 200 Hz) was analyzed for automatic detection of R waves with the software Hypnolab utilizing a simple threshold plus first and second derivative algorithm. R–R intervals from each epoch were calculated and their value was obtained at regular intervals of 1 s by linear interpolation of the measured values, for the first 256 s which were utilized for all subsequent analysis steps.

First of all, a series of time-domain measures was calculated: (i) mean R–R value; (ii) standard deviation of all R–R intervals (SDNN) which reflects all the cyclic components responsible for variability and is mathematically equal to total power of spectral analysis (see below); (iii) the square root of the mean of the sum of the squares of differences between adjacent R–R intervals (RMSSD), number of pairs of adjacent R–R intervals differing by more than 50 ms in the entire epoch (NN50), and percentage of NN50 among the total R–R intervals (pNN50); all these parameters measure short-term variation and estimate high frequency variations in heart rate.

The interpolated R–R interval tachograms were also processed by means of a Fast-Fourier Transform (FFT) algorithm and the following spectral parameters were obtained:

(i) power in very low-frequency range (VLF), <0.04 Hz,
(ii) power in low-frequency range (LF), 0.04–0.15 Hz,
(iii) power in high-frequency range (HF), 0.15–0.4 Hz,
(iv) total power (VLF + LF + HF),
(v) LF% (LF power in normalized units: LF/(total power − VLF) × 100,
(vi) HF% (HF power in normalized units: HF/(total power − VLF) × 100,
(vii) LF/HF (ratio LF/HF).

It is usually accepted that the activities of the ANS and peripheral nervous system (PNS) are reflected in the LF and HF bands of HRV while, with approximation, the LF/HF ratio is used to quantify the degree of sympathovagal balance. The VLF band is measured but not considered further for its unclear significance.

2.5. Statistical analysis

Data from five participants (three of them were adolescents older than 18 years) were excluded from final analysis due to intermittent signal artifacts, resulting in a final sample for analysis of 60 adolescents (33 NW and 27 OW). Data are presented as mean ± standard error of the mean (SEM) for parametric variables and median with interquartile range for non-parametrically distributed variables. Because R–R interval and spectral values of HRV differ greatly among individuals, R–R interval was square-root transformed and spectral power of HRV variables (for VLF, LF, HF, and LF/HF ratio) log-transformed; however, for clarity, HRV variables (except LF/HF) are reported as mean values of untransformed data. Group differences (OW vs NW) on RR intervals and HRV estimates were assessed according to sleep–wake stages and thirds of the night, using a mixed-effects linear regression model, allowing the assessment of the effect of each variable and its interaction regarding the outcome. Regression models included HRV estimates, as dependent variables, and group (OW vs NW) as the independent variable, with age, gender, and sleep time and efficiency as covariates. Analyses were performed by thirds of the night and each sleep–wake stage. The software STATA 13.1 (Stata Corporation, College Station, TX) was used in all analyses, and the GraphPad Prism v.6.0 (GraphPad Software, San Diego, CA, USA) was used for processing figures. Statistical significance was set at α-level ≤ 0.05.

3. Results

Background, anthropometric, and metabolic parameters are shown in Table 1. Groups were similar for age and gender distribution. As expected, body weight, BMI z-score, and waist circumference were higher in the OW group. Fasting glucose and insulin as well as total cholesterol, low-density lipoprotein and high-density lipoprotein cholesterol were within the normal range and did not differ between groups. Blood pressure also showed no differences between groups (Table 1).

Table 1
Background characteristics.

	Overall	NW	OW	*p*[b]
	(*N* = 60)	(*N* = 33)	(*N* = 27)	
Age (years)	15.7 ± 0.09	15.7 ± 0.1	15.7 ± 0.1	0.48
Gender (M/F)	35/26	21/12	15/12	0.49
BMI z-score[a]	0.9 ± 0.1	0.2 ± 0.1	1.8 ± 0.1	**0.001**
Waist circumference (cm)	81.2 ± 1.3	75.2 ± 1.2	88.2 ± 1.8	**0.001**
Fasting glucose (mg/dL)	88.9 ± 1.1	88.6 ± 1.7	89.5 ± 1.3	0.675
Fasting insulin (IU/mL)	7.1 ± 0.5	6.4 ± 0.6	8.2 ± 0.9	0.129
HOMA-IR	1.5 ± 0.1	1.4 ± 0.1	1.8 ± 0.2	0.111
Total cholesterol (mg)	153.6 ± 3.3	151.6 ± 4.3	156.3 ± 5.4	0.507
LDL cholesterol (mg)	93.7 ± 3.1	94.0 ± 3.8	93.2 ± 5.4	0.893
HDL cholesterol (mg)	41.0 ± 1.3	41.1 ± 1.8	40.4 ± 2.2	0.718
SBP (mmHg)	112.8 ± 2.0	110.6 ± 2.0	115.3 ± 3.6	0.276
DBP (mmHg)	66.5 ± 0.9	65.9 ± 1.2	67.2 ± 1.4	0.494

Bold *p* value denotes significant difference between groups.
BMI, body mass index.
Data are reported as mean ± standard error of the mean (SEM) unless otherwise specified.
DBP, diastolic blood pressure; F, female; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment for insulin resistance index (Matthews et al. *Diabetologia* 1985; 28:412–9 [36]); LDL, low-density lipoprotein; M, male; NW, normal weight; OW, overweight; SBP, systolic blood pressure.
[a] BMI z-score adjusted by age and gender, according to WHO reference growth standards.
[b] *p*-values obtained with the Student's *t*-test and chi-squared for continuous and categorical variables, respectively.

Table 2
Sleep organization.

PSG variables	NW (N = 33)	OW (N = 27)	p
Sleep onset time (h:min)	23:30 ± 0:31	23:23 ± 0:37	0.45
Sleep ending time (h:min)	7:44 ± 0:50	7:35 ± 0:54	0.07
Sleep period time (min)	496.4 ± 9.2	493.4 ± 13.0	0.43
Total sleep time (min)	482.6 ± 8.5	473.1 ± 14.8	0.29
Sleep efficiency (%)[a,b]	98.8 (3.5)	98.3 (7.5)	0.28
Sleep latency (min)[a]	8.5 (10.5)	7.9 (11.9)	0.73
Sleep cycles (N)	5.1 ± 0.4	4.2 ± 0.2	0.09
REM sleep latency (min)[a]	95.5 (71.0)	103.9 (90.5)	0.46
WASO (%)[c]	1.1 (3.5)	1.6 (7.5)	0.18
S1 (%)[d]	3.83 (4.5)	5.64 (3.4)	0.10
S2 (%)[d]	52.3 ± 0.9	53.7 ± 1.3	0.18
SWS (%)[d]	23.0 ± 0.9	22.2 ± 1.1	0.29
REM (%)[d]	19.8 ± 0.5	18.0 ± 0.8	**0.04**
OAHI[e]	0.9 (1.5)	0.7 (0.6)	**0.001**
AHI	1.3 ± 0.2	1.1 ± 0.1	0.40
Central apnea index (N/h)	0.2 ± 0.07	0.1 ± 0.06	0.23
SpO_2 (%)	96.2 ± 0.1	96.1 ± 0.2	0.46
Snoring index (N/h)	0.9 ± 0.3	0.2 ± 0.1	0.11

Bold *p* value denotes significant difference between groups.
Data are reported as mean ± standard error of the mean (SEM) unless otherwise specified. AHI, apnea hypopnea index (N events/h of TST); NW, normal weight; OW, overweight; PSG, polysomnographic; REM, rapid-eye-movement sleep; S1, non-rapid-eye movement (non-REM) sleep stage 1; S2, non-REM sleep stage 2; SpO_2, oxygen saturation level; SPT, sleep period time; SWS, slow-wave sleep; TST, total sleep time.
[a] Median (interquartile range).
[b] Sleep efficiency: [(TST/SPT) × 100].
[c] WASO: Wakefulness during SPT, expressed as a percentage of SPT.
[d] Expressed as a percentage of total sleep time.
[e] OAHI: obstructive apnea–hypopnea index (N events/h of TST).

3.1. Sleep organization

Conventional sleep parameters are shown in Table 2. Sleep time and sleep efficiency were within the expected range and without differences between groups. Groups were similar regarding the total amount of sleep and the number and duration of episodes in all non-REM sleep stages. Compared with the NW group, the OW group showed reduced REM sleep percentage ($p = 0.04$, Table 2).

3.2. HR time-domain estimates

R–R intervals according to sleep stages were shorter in the OW group (Fig. 1). Between-group stage-dependent differences were found in T1 for WASO ($p = 0.008$), Stage 2 ($p = 0.02$) and SWS ($p = 0.07$), and in T2 for S1 ($p = 0.04$). The same differences were found in T3 (Fig. 1).

The OW group showed lower RRSD values as a function of sleep–wake stages: in T1, for SWS ($p = 0.03$) and REM sleep ($p = 0.007$), in T2, for stage 2 ($p = 0.03$), SWS ($p = 0.03$), and REM sleep ($p = 0.0001$), and in T3, for stage 2 ($p = 0.0009$) and REM sleep ($p = 0.03$). The OW group had lower values for RMSSD during WASO in both T1 and T3 ($p < 0.0001$) and for NN50 and pNN50 during the night as a whole (both $p < 0.04$).

3.3. HRV frequency domain estimates

VLF power showed an increasing value trend, with the lowest values in SWS and the highest values in WASO (Fig. 2). The only between-group difference was higher VLF power during WASO for the whole night ($p = 0.01$) and T1 ($p = 0.0001$) in the OW group (Fig. 2). LF power showed a decreasing value trend from Wake to SWS, rising again during REM sleep (but still lower compared with Wake values). The OW group showed higher LF power during WASO in both T1 and T2 ($p < 0.007$, Fig. 2B) and REM sleep in T2 ($p = 0.002$).

Increasing values of HF power from Wake to SWS characterized both groups. The OW group showed lower HF power during WASO in T1 and T2 (both $p < 0.0001$). Finally, the LF/HF ratio showed a decrease from Wake to SWS, rising again in REM sleep (but still

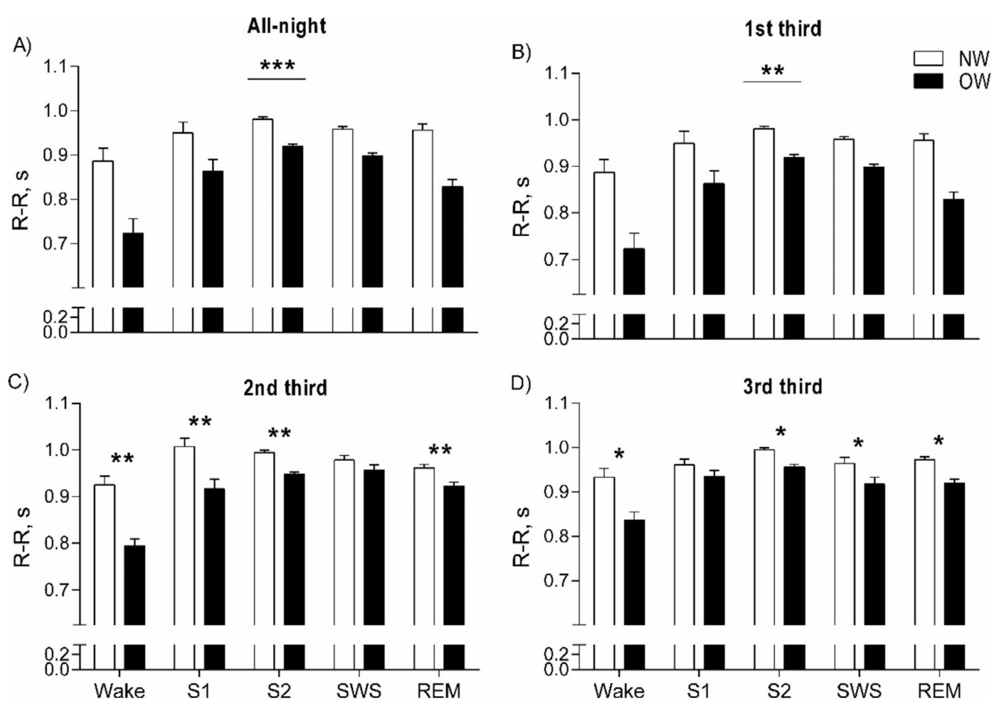

Fig. 1. Mean R–R interval by sleep–wake stages. Data are shown as mean ± standard error of the mean (SEM). Between-groups differences: ***$p < 0.001$ in (A), and **$p < 0.01$ in (B); **$p < 0.01$ in (C); *$p < 0.0001$ in (D). In (A) and (B), horizontal line denotes significant group differences for all sleep–wake stages. First, second and third consecutive thirds of the sleep period time; NW, normal weight; OW, overweight; REM, rapid-eye movement sleep; S1, non-REM sleep stage 1; S2, non-REM sleep stage 2; SWS, slow-wave sleep; WASO, wakefulness after sleep onset.

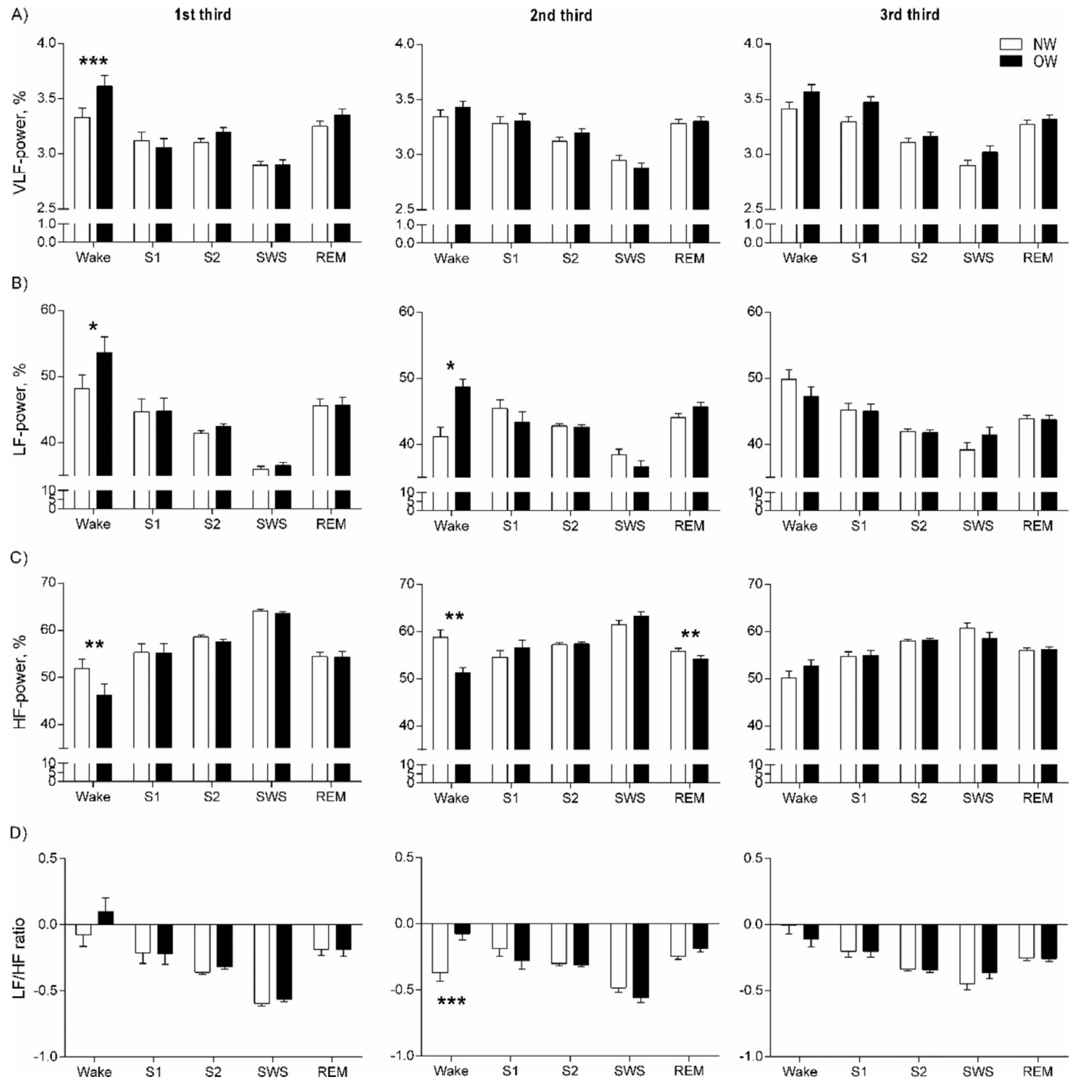

Fig. 2. Heart rate variability (HRV) frequency-power by sleep–wake stages. Data are shown as mean ± standard error of the mean (SEM). Between-groups differences: $^{***}p = 0.0001$ in (A); $^{*}p < 0.05$ in (B); $^{**}p < 0.01$ in (C); $^{***}p < 0.0001$ in (D). First, second and third consecutive thirds of the sleep period time; NW, normal weight; OW, overweight; REM, rapid-eye movement sleep; S1, non-REM sleep stage 1; S2, non-REM sleep stage 2; SWS, slow-wave sleep; WASO, wakefulness after sleep onset.

lower compared with Wake values); the only LF/HF ratio difference between groups was the higher ratio for the NW group during WASO in T2 ($p = 0.007$, Fig. 2D).

4. Discussion

The results of this study support our original hypothesis that altered sleep-related HRV patterns characterize ANS dysregulation in OW individuals. We aimed to compare cardiac autonomic activity during night-time sleep–wake stages between otherwise healthy OW and NW adolescents. Our main findings indicate shorter RR intervals throughout the night and for sleep stages in OW adolescents. Time-domain indicators of PNS activity or vagal tone, such as RRSD and RMSSD values, were reduced in OW adolescents during non-REM sleep stages S2 and SWS and REM sleep. Altogether, our results of shortened RR intervals during the whole night and stage-specific group differences in LF and HF power in OW adolescents suggest a reduced parasympathetic tone throughout night-time sleep in this group even before the onset of metabolic alterations.

Studies reporting altered sympathetic tone and/or vagal tone in association with increased BMI [37,38] have been performed without differentiating sleep–wake stages [38,39]. For instance, Martini et al. [40], showed lower values for HF, LF/HF ratio, and time-domain parameters during the 24-h period in obese adolescents compared to healthy controls. Kaufman et al. [41], studied a sample of 36 children (mean age 11.5 years) during a morning short resting (wake) episode and concluded that obese children had higher LF power, higher LF/HF ratio, and reduced HF power compared with NW children (without differences between OW and obese children). More recently, similar findings were reported in a sample of 12-year-old NW and OW children [42]. Rabbia et al., added interesting findings to this relationship by reporting a sympathetic dominance (lower HF, higher LF, and increased LF/HF ratio) during night-time in adolescents with recent-onset obesity (less than four years) relative to controls [38]. Other studies supported a reduced night-time HF power and estimated vagal activity during night-time in obese adolescents [40].

To the best of our knowledge, this is the first study to compare cardiac autonomic modulation as a function of night-time sleep–wake stages in NW and OW adolescents. Focusing on all-night HRV analysis during sleep, our findings are in line with the reports mentioned above. Indeed, OW adolescents were characterized by higher VLF power and LF power and reduced HF power, particularly in the first two-thirds of the night, depending on sleep–wake stages. Further, time-domain RRSD and RMSSD parameters were also reduced in OW adolescents. We also found consistently shorter RR intervals (faster HR) in the OW group for the whole night and all sleep–wake stages. Altered sympathetic and vagal tone during the early part of the night could reflect a carry-over effect of the disrupted ANS balance during the wake preceding sleep onset in OW subjects. Another possibility, not mutually exclusive, is a weaker potential of sleep stage regulatory processes to modulate cardiac autonomic tone in OW adolescents and hence, longer time to establish the night-time expected ANS balance in this group. For instance, the increased baroreflex sensitivity and rapid and substantial peripheral vasodilatation involved in decreasing sympathetic tone and increasing parasympathetic tone at wake–sleep transition could be less efficient in the presence of OW [43,44].

Reports for LF power in OW adolescents are controversial with either reduced or increased values in obese individuals [37,39]. Given that LF power relates to both PNS and SNS subsystems [45], we cannot exclude that differences in LF power could correlate, in part, to a diminished sinus node sensitivity to blood pressure oscillations in OW subjects [46].

Alterations of the ANS can underlie the metabolic consequences of disturbed and/or short-sleep [24,47]. It has been shown that an autonomic imbalance contributes to weight gain and obesity in children and adolescents [37,48,49]. Low HRV and sympathetic dominance are associated with metabolic disorders, including metabolic syndrome in adolescents [50,51]. Because there are close connections between metabolic and autonomic domains and an ANS dysfunction (through increased sympathetic activity) is a common underlying condition in obesity, sleep disorders and insulin resistance, the role for regular sleep–wake patterns appears relevant for both ANS and metabolic regulations [6]. Rodríguez-Colón et al. [52], have reported that greater variability of habitual sleep duration and sleep efficiency – but not sleep duration or sleep efficiency itself – was associated with decreased HRV in healthy adolescents, highlighting the relevance of adequate sleep patterns for optimal cardiac autonomic function. As suggested by others [53], not only sleep duration but also other features of sleep, such as sleep quality, timing or regularity, need to be considered for a better understanding of the role of sleep in ANS and pediatric obesity throughout development.

In our study, sleep architecture was quite similar in both groups and within the expected range. However, diminished REM sleep was observed in OW adolescents. These subtle changes are in line with previous reports by our group and others in OW and obese children and adolescents [21,22,54]. It is unlikely that these differences in sleep organization relate to differences observed in HRV parameters because sleep efficiency and sleep episode duration were similar in both groups and were included as covariates in all analyses. Another consideration is that we observed altered HRV regulation throughout the night and for different sleep stages, in a group of otherwise healthy OW adolescents. These results suggest that sleep-related changes in HRV regulation might appear before the onset of overt metabolic derailments. In fact, obese adolescents without metabolic complications showed no cardiac ANS imbalance during a morning assessment while awake [55].

Regarding the limitations of our study, daytime HRV patterns were not assessed thus restricting the interpretation of the ANS circadian modulation. Given the cross-sectional nature of our study, we were unable to determine whether altered cardiac autonomic regulation during sleep preceded weight gain in this group of adolescents or vice versa. A strength of the study is the use of PSG, the gold-standard method for sleep evaluation. PSG allowed assessment of HRV patterns according to sleep–wake stages and throughout the night. Because all participants in our study were otherwise healthy, with a narrow age range, and without any medication and free from sleep disorders, it is unlikely that such factors accounted for our findings. The same is the case for sleep restriction, another well-known modifying factor of ANS tone [56], because all participants were assessed following their usual sleep–wake rhythm.

5. Conclusions

In summary, our results showed altered cardiac ANS tone during night-time sleep–wake stages in otherwise healthy OW adolescents. Because differences between groups prevailed during the early portions of the night, we suggest that sleep mechanisms required to reverse the ANS balance at wake–sleep transitions may be less efficient in OW adolescents. Further studies should be undertaken to elucidate the role of an altered autonomic regulation during sleep for the development of overweight and related metabolic disturbances.

Author contributions

P.P., C.A. and B.L. designed the study; R.C., M.G., S.D.-A. conducted the research; R.C., M.G., O.R., and S.D.-A. analyzed data; R.C., C.A., M.G., S.D.-A., L.C., C.H., R.F., B.L., and P.P. interpreted the data. R.C. and P.P. wrote the paper. All authors critically reviewed the paper and approved the final version.

Conflicts of interest

None.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.06.008

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