

Cyclic Variation in Heart Rate during Sleep in Four Recordings of up to 13 Years in Elderly Adults

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Abstract

To characterize changes in nighttime cyclic variation in HR (CVHR) with advancing age in older adults, CVHR was quantified for N=56 adults with 2 Holter recordings 5 yrs apart (CHS1 and CHS 2) in the Cardiovascular Health Study (CHS) and 2 overnight polysomnograms 5 yrs apart in the Sleep Heart Health Study (SHHS1 and SHHS2) using MatLab. Baseline age was 71±3yrs. The number of CVHR events was also normalized to time in bed (CVHR Index). CVHR Index did not change across recordings, but males had higher values ($p=0.009$). Mean HR increase during CVHR was similar in the first 3 recording but declined on the last ($p<0.02$). CVHR duration increased, but CHS1 vs. CHS2 and SHHS1 vs. SHHS2 were NS (rest, $p<0.007$). We conclude that CVHR is frequent at night in older adults, but results suggest an age-related trend towards decreased magnitude and longer durations of HR arousals, possibly due to the aging of the autonomic nervous system.

1. Introduction

Cyclic variation of heart rate (CVHR) describes a phenomenon observed primarily during sleep where there are visible cycles of increasing and decreasing heart rate. CVHR represents repeated autonomic arousals, even though the individual is asleep. The clinical significance of these arousals in terms of contributing to daytime sleepiness or cardiovascular risk is unknown. Apneas and hypopneas that occur during sleep are associated with CVHR, as are periodic limb movements.¹ When respiratory events occur, a sharp rise in heart rate arousal occurs when the individual “wakes.” Often breathing amplitude is greater during this period. Then the individual falls back to sleep and heart rate returns to baseline, whereupon a new respiratory event occurs and the cycle begins again. However, CVHR may occur in the absence of events that are scored during routine

polysomnography, perhaps representing subclinical respiratory events that do not reach the relatively arbitrary thresholds used for scoring.² For example, a respiratory event lasting 10 seconds or more is scored, but an event that is 9.5 seconds is not. Heart rate arousals also occur for other unknown reasons and when associated with EEG changes above a certain also arbitrary threshold are described as “arousals for no apparent reason.” For this reason, we propose that quantification of CVHR might provide additional and specific information about autonomic arousals during sleep that may increase the clinically-relevant information available from Holter recordings or from PSGs. In the current study, we explored changes in CVHR over time in a group of elderly individuals with 4 continuous ECGs recorded during sleep over a period of up to 13 years.

2. Methods

Cyclic variation in heart rate (CVHR) during time in bed was quantified for N=56 adults with 2 Holter recordings five years apart (CHS1 and CHS 2) as part of their participation in the Cardiovascular Health Study (CHS).³ Participants also had two overnight polysomnograms (PSGs) five years apart as part of their participation in the Sleep Heart Health Study (SHHS1 and SHHS2).⁴ The first PSG was recorded approximately 1 year after the second Holter recording in the CHS. Baseline age was 71±3yrs, 19M, 37F. Time in bed for the Holter recordings was determined using methods developed in this laboratory. Time in bed for the PSGs was based on information from “lights out” and “wake” times usually stored with the PSG. When lights out had not been recorded, bed time was estimate from changes in the PSG signals. A custom-designed algorithm in MatLab (The Mathworks, Natick, MA) quantified CVHR during time in bed for each recording. CVHR was defined *a priori* as a ≥ 6 bpm increase in HR, lasting ≥ 10 and ≤ 60 sec. Automatic detection of the start, peak and end heart rate and time of every CVHR cycle was

performed and then overread using an interactive editor and verified by a second reader. Figures 1-4 show examples of CVHR detection over 4 recordings in a single participant. Each figure represents about 30 minutes of sleep from approximately the same time period. The start, peak and end of each CVHR cycle are indicated by dots.

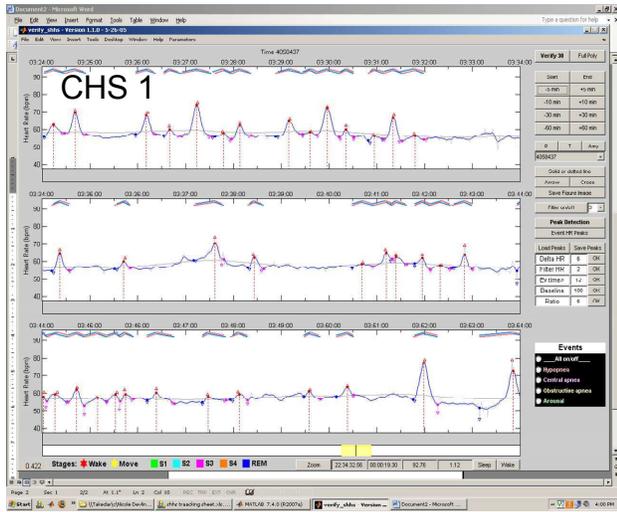


Figure 1. Thirty minutes of CVHR patterns from the baseline CHS Holter recording.

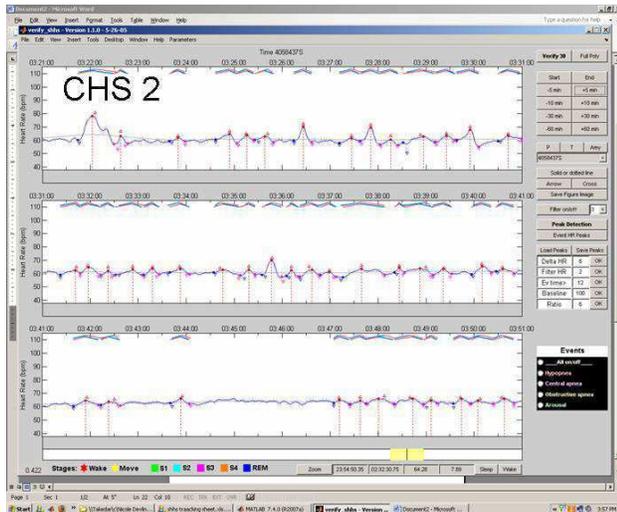


Figure 2. Thirty minutes of CVHR patterns from the second CHS Holter recording. Same participant and approximately the same time period as Figure 1.

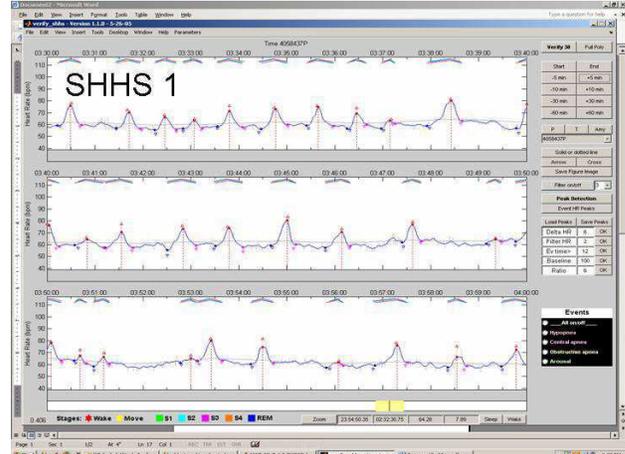


Figure 3. Thirty minutes of CVHR patterns from the first SHHS PSG in the same participant during approximately the same time period as Figures 1 and 2. This pattern is consistent with severe sleep apnea.

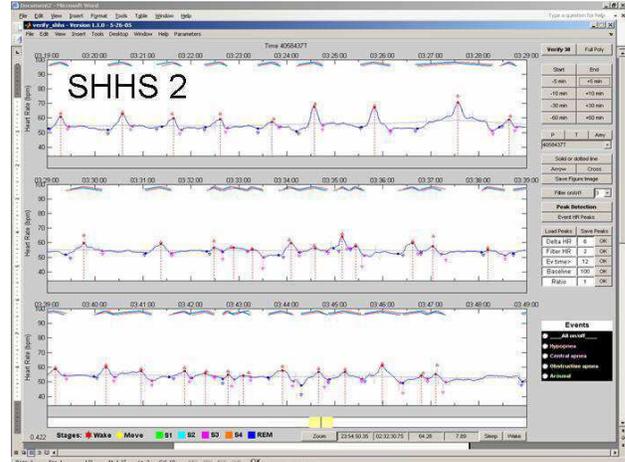


Figure 4. Thirty minutes of CVHR patterns from the second SHHS PSG in the same participant as Figures 1,2,3 and during approximately the same time period.

The average heart rate (HR) increase during CVHR cycles, the average duration of CVHR cycles and the total number of CVHR cycles was determined from the start, peak and end heart rates and times for each recording. Cycles with heart rate changes <6 bpm or durations <10 s were excluded from these calculations. The number of CVHR cycles was also normalized to time in bed to derive a CVHR index. Results were compared by gender. ANOVA with repeated measures compared results from the 4 recordings. Correlations between recordings were also determined. SPSSPC 14 (SPSS, Chicago, IL) was used for all statistical analyses.

3. Results

Table 1 shows results as mean \pm SD and ranges. Mean HR increase during CVHR was similar in the first 3 recordings but declined significantly on the last ($p < 0.022$ for all comparisons between the last and other recordings). The magnitude of HR increases was significant correlated for all recordings (range $r = 0.32$ for to $r = 0.71$, $p < 0.017$). Arousal duration increased across recordings, but CHS1 vs. CHS2 and SHHS1 vs. SHHS2 were not significant (rest, $p < 0.007$). Inter-individual correlations of arousal durations were lowest between the first and last recordings ($r = 0.3$, $p = 0.026$) and moderate for all other comparisons ($p < 0.007$). There was no gender effect on mean HR increase or on arousal duration. Mean CVHR Index (CVHR/hr) did not change across recordings. As shown in Figure 5, mean values for CVHR Index were 6-14 events/hr higher for males at all time points, but differences were significant for the first two recordings only. Median CVHR Index tended to decrease between the first and last recordings from 60.2 on the first to 58.8 events/hr on the last recording in females, while median CVHR increased among males from 67.8-73.7 events/hr. CVHR Index was moderately correlated between the first 3 recording ($r > 0.54$, $p < 0.001$), but was not significantly correlated with CVHR Index on the last recording.

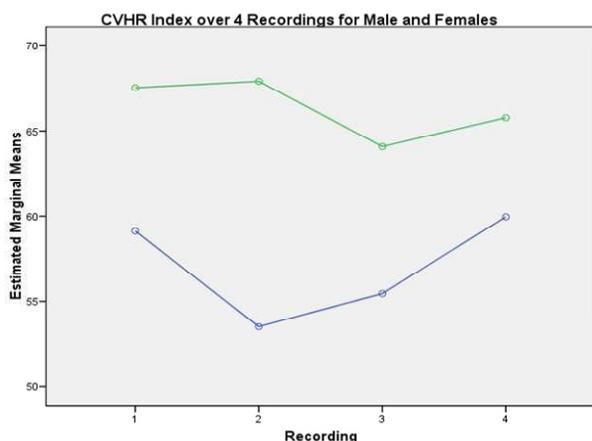


Figure 5.

	CHS1	CHS2	SHHS1	SHHS2
HR Increase	7.8 \pm 1.4 (5.4-11.2)	7.8 \pm 1.9 (4.6-16.3)	7.7 \pm 1.7 (4.1-12.5)	6.9 \pm 1.9 (3.7-14.0)
Arousal Duration	24.0 \pm 2.0s (20-39)	24.3 \pm 2.4s (21-34)	25.3 \pm 2.3s (19-31)	25.5 \pm 3.7s (19-40)
CVHR Index	62 \pm 15 (31-107)	58 \pm 17 (9-98)	54 \pm 18 (20-105)	62 \pm 23 (6-108)

4. Discussion and conclusions

CVHR is frequent at night in older adults and is easily quantifiable. An average of about 60 events per hour was counted and this mean value did not change over the 13 year follow up. However, there was considerable variation among participants and results for the last recording were less consistent than those of prior recordings, suggesting greater variation with extremely advanced age. Average heart rate increases were substantial, about 7-8 bpm and average heart rate increases with CVHR of up to 16 bpm were observed, suggesting that there is significant periodic activation of the autonomic nervous system during sleep in older adults. Results also suggest an age-related trend towards decreased magnitude of HR arousals and longer arousal durations, possibly due to the aging of the autonomic nervous system. Our results support the potential of this measure to capture information about sleep that is not contained in traditional Holter recordings or PSGs. Our prior work has shown that although events like apneas, hypopneas or leg movements usually cause CVHR, many heart rate arousals are not captured by standard sleep scoring.

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References

- [1] Stein PK, Duntley SP, Domitrovich PP, Nishith P, Carney RM. A Simple Method for Detecting Sleep-Disordered Breathing Using Holter Monitoring. *J of Cardiovascular Electrophysiology* 2003;14:453-4.
- [2] Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep states of human subjects. Los Angeles, CA. Brain Information Service/Brain Research Institute 1968.
- [3] Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, Kuller LH, Manolio TA, Mittelmark MB, Newman A, et al. The Cardiovascular Health Study: design and rationale. *Ann Epidemiol.* 1991;1:263-76.
- [4] Quan SF, Howard BV, Iber C, Kiley JP, Nieto FJ, O'Connor GT, Rapoport DM, Redline S, Robbins J, Samet JM, Wahl PW. The Sleep Heart Health Study: design, rationale, and methods. *Sleep.* 1997;20:1077-85.

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