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A Scoping Review of Current Methodologies of Measuring Cardiopulmonary Coupling and their Limitations in Sleep Apnea Detection

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Abstract—**Cardiopulmonary coupling (CPC) analysis is a non-invasive technique increasingly used to evaluate the autonomic nervous system's control over heart and respiratory functions, particularly during sleep. This review delves into current methods of CPC analysis, including the preprocessing of electrocardiogram (ECG) signals, extraction of meaningful measures, and features, and the use of machine-learning classification for sleep-related diseases. The review also examines different patient cohorts in the existing literature and the efficiency and accuracy of automated sleep apnea detection, highlighting the limitations and potential of these methodologies in clinical settings.**

Keywords— **Sleep apnea, Cardiopulmonary Coupling, Electrocardiography (ECG), ECG/PPG-derived respiration, Fourier Transform.**

I. INTRODUCTION

As the scientific understanding of sleep deepens, innovative technologies have emerged to unravel the complexities of sleep disorders, among which sleep apnea (SA) stands out as a significant concern [1]. Detection of SA through a full-night polysomnography is expensive, labor-intensive, and time-consuming [2-3]. An alternate promising tool - Cardiopulmonary Coupling (CPC) analysis, offers unique insights into the dynamic interplay between cardiac and respiratory systems during sleep [1,4-5]. CPC uses an electrocardiogram (ECG) or photoplethysmography input to derive ECG/photoplethysmography -derived respiration (EDR) signals and the normal-to-normal sinus (N-N) interval [1,6]. From frequency-domain to time-domain analyses, there are various approaches utilized to extract meaningful information from the complex physiological signals in CPC analysis [7]. Understanding these analytical methods is crucial as it lays the foundation for accurate interpretation and application of CPC data in the clinical setting. Here we aim to explore existing methods of CPC analysis including preprocessing, feature extraction, and machine-learning classification. This review also aims identify any population bias that may impact the biological conclusions presented and the application of artificial intelligence for automated SA detection.

II. METHODS

We initially searched for CPC analysis on Google Scholar; the search was sequentially narrowed using SA and transform-related keysearch words (listed below). A similar approach was applied to PubMed and Web of Science. Duplicates were removed using reference manager software. Reviews and web-unavailable papers were excluded. The search was refined to include keywords specific to ECG-based diagnostic systems, signal processing, time-domain analyses, frequency-domain analyses, and/or machine-learning classifications of SA. Titles and abstracts were scanned for descriptions of CPC methodologies. The main text of selected papers was screened to ensure a sufficient description of the methodology. We selected papers applying transforms for SA detection, classification, or comparison to traditional diagnostic methods. Keywords: ("sleep apnea" OR "sleep-disordered breathing" OR "obstructive sleep apnea" OR "central sleep apnea" OR "hypopnea" OR "apnea" OR "apnea-hypopnea index") AND ("electrocardiography" OR "heart rate variability") AND ("signal processing" OR "signal filtering" OR "time-domain analysis" OR "frequency-domain analysis" OR "threshold-based algorithms" OR "Fourier-transform" OR "synchrosqueezing transform" OR "continuous wavelet transform", "short-time Fourier transform", "Hilbert–Huang transform" OR "machine learning")

III. RESULTS

There were 66,400 search results for CPC analysis in total. The majority of the papers published used the Fourier Transform (FT) - based CPC analysis technique; however, other transforms have been utilized to address some of the shortcomings of the traditional FT (Table 1).

Table 1: List of papers using various CPC analyses.

Paper	CPC Method	Purpose/Objective	Results
Thomas et al. (2005) [4]	Fourier transform (FT)	Assessing a novel approach for CPC	Highly aligns with CAP states
Thomas et al. (2007) [8]	Fast-Fourier transform (FFT)	Distinguishing obstructive, central or complex SA.	Effectively differentiates SA types.
Quiceno-Manrique et al. (2009) [10]	Short-time Fourier transform (STFT)	Apply time-frequency analysis for OSA detection.	92.67% accuracy on per-minute base.
Guo et al. (2011) [9]	Fast-Fourier transform (FFT)	Assess CPC method in pediatric SDB.	Highly correlates with respiratory abnormality in pediatric SDB.
Liu et al. (2012) [11]	Hilbert–Huang transform (HHT)	HHT-CPC analysis to detect severity of SDB	Finer temporal and frequency resolutions.
Lin et al. (2021) [12]	Continuous Wavelet transform (CWT)	Automate SA classification system	High resolution in two windows for different frequency bands.
Wang et al. (2023) [14]	Synchrosqueezing Transform Algorithm (SST)	Refine CPC measurements with SST.	83% accuracy per-minute base.

A. Fourier Transform

FT, a key tool in signal processing, breaks down signals into their frequency components [8]. The original CPC analysis algorithm by Thomas et al. (2005) is based on FT, assessing sleep using automated CPC measures. The algorithm, trained on the American Academy of Sleep Medicine-accredited Sleep Disorders Center, consisted of 70 polysomnograms [4]. Following QRS algorithm-based R-R interval and EDR extraction, signals were decomposed into sinusoidal oscillations [4]. Coherence was calculated for synchronized oscillations and cross-spectral power was calculated for coupled signals, at a given frequency [4]. 2 Hz resampling with cubic spline interpolation maintained signal consistency [4]. Cross-spectral power and coherence were computed for three overlapping 512-sample sub-windows over a 1024-sample window (~8.5 minutes) advanced by 256 samples (~2.1 minutes) for subsequent analyses [4]. The training set comprised 20 males and 15 females (average age: 46 ± 12, BMI: 28 ± 4 kg/m^2), and the test set had 28 males and 7 females (average age: 49 ± 18, BMI: 31 ± 5 kg/m^2) [4].

Following the methodology of [4], Thomas et al. (2007) targeted detection of elevated-low-frequency coupling patterns, indicative of apneas and hypopneas [8]. Training dataset included 70 polysomnograms from the PhysioNet Sleep Apnea Database (males and females aged 27 to 63) [8]. Sleep Heart Health Study-I contributed 3989 polysomnograms and PhysioNet BIDMC Congestive Heart Failure Database added 15 subjects with severe congestive heart failure for further algorithm training [8].

Guo et al. (2011) utilized FFT-based CPC analysis to assess correlation of CPC metrics with nasal-pressure based apnea-hypopnea scoring [9]. Following the methodology of [4], they substituted an automated beat detection algorithm for the QRS algorithm [9]. In the group with mean nasal-flow respiratory disturbance index of 36.1/h, CPC correctly diagnosed 40% of individuals in the non-severe group, and 94.3% in the severe group [9]. The sample population included 63 participants (2-12 years) [9]. The weight, BMI, and sex of participants were not reported [9].

Quiceno-Manrique et al. (2009) utilized Short Time Fourier Transform (STFT) for time-frequency analysis of heart rate variability signals in ECG recordings to detect obstructive sleep apnea (OSA) [10]. Following QRS detection, time-frequency analysis was conducted using Cohen's class of quadratic distributions [10]. To smooth out artifacts, window functions were applied and Linear Frequency Cepstral Coefficients were used for additional signal processing [10]. Dynamic features were analyzed using a k-nearest neighbor classifier combined with principal component analysis, enabling differentiation between normal and pathological ECG signals [10]. The sample population was not described, however, the database consists of 35 recordings [10].

B. Hilbert-Huang Transform

The Hilbert-Huang Transform (HHT) is an adaptive method used to analyze non-linear and non-stationary time series data [11]. Unlike FT, which assumes linearity and stationarity, HHT employs Empirical Mode Decomposition to decompose complex data sets into a finite number of intrinsic mode functions, capturing natural oscillation mode [11]. Hilbert spectral analysis provides time-frequency data for each intrinsic mode function, enhancing SA detection and severity assessment using ECG data. Liu et al. (2012) used this method by resampling R-R intervals and EDR at 2 Hz and decomposing them into intrinsic mode functions. The resulting HHT-CPC sleep spectrum, analyzed for power and coherence, provides high resolution. This study validated statistically and demonstrated HHT's superiority over traditional FT-based methods in analyzing sleep architecture and determining SA severity. The sample population comprised 69 subjects from PhysioNet clinical database (aged 27 to 63; 56 males and 13 females) [11].

C. Continuous Wavelet Transform

Continuous Wavelet Transform (CWT) analyzes time and frequency details of ECG signals simultaneously, allowing for the detection of variable and transient characteristics of SA [12]. Lin et al. (2021) integrated machine learning and a bag-of-features technique [12]. The algorithm tested different spectrogram window times (10 and 60 seconds) and frequency bands (0.1–50 Hz, 8–50 Hz, 0.8–10 Hz, and 0–0.8 Hz) demonstrating high classification accuracy and temporal resolution [12]. The sample population consisted of 33 participants with varying degrees of SA severity [12].

Li et al. (2023) integrated CWT into the standard CPC algorithm to evaluate age-related differences in sleep signals, offering refined time-frequency resolutions for understanding sleep patterns [13]. Both respiratory and RR signals were uniformly interpolated to 8 Hz [13]. The Morlet wavelet was chosen for its effectiveness in analyzing the time-frequency characteristics of the signals with symmetric padding to address boundary effects [13]. The sample population included a younger cohort (aged 21 to 34 years), and an elderly cohort (68 to 81 years), with an equal number of healthy males and females [13].

D. Synchrosqueezing Transform

Synchrosqueezing Transform-Coupled Cardiopulmonary (SST-CPC) analysis outperforms traditional FT-based methods for per-minute sleep-disordered breathing (SDB) detection [14]. SST-CPC offers enhanced temporal and frequency resolution without relying on stationary signal assumptions [14]. Wang et al. (2023) preprocessed ECG signals with bandpass and Savitzky-Golay filters, Pan-Tompkins algorithm for R-peaks detection and resampled at 4 Hz [14]. Applying CWT to RR intervals and EDR, they used a phase transform for instantaneous frequencies and the SST algorithm enhanced the time-varying frequency representation [14]. The resulting SST spectrogram facilitated feature extraction, aiding in the classification of physiological events, and enhancing ML algorithm-based SA detection [14]. Wang et al. (2023) utilized the PhysioNet Apnea dataset, consisting of individuals across various ages and severities of SA [14].

IV. Discussion

This review explores existing methods in CPC analysis including preprocessing, feature extraction, and ML classification. The traditional method, used by [4] detects peak points, however, the 8-minute time window may blur rapid state alterations [4]. Many studies since have adopted a similar methodology. Thomas et al. (2007) found a strong correlation between the algorithm's detection of elevated LFC and human scoring of apneas and hypopneas, with limitations including the need for further validation of the algorithm's ability to classify hypopneas accurately [8]. The presence of narrow spectral band elevated-low-frequency coupling emerged as a predictive factor for the induction of complex SA during positive airway pressure titration [8]. Guo et al. (2011) reported limitations in the method's non-specificity and its focus on severe cases of SDB [9]. Quiceno-Manrique et al. (2009) achieved comparable accuracy, with enhanced time-frequency resolution [10]. The method's accuracy was comparable only when tested with the best-selected observations, suggesting a possible reduction in performance with less ideal data sets [10]. In another study, researchers used STFT to extract meaningful features from time-varying signals, achieving 96.9% sensitivity and 97.1% specificity in fall detection [15].

The FT presupposes a stationary signal, often resulting in unsatisfactory frequency and time resolution [4]. CWT effectively manages irregularities in ECG signals, providing high time and frequency resolution for accurate SA identification [12]. CWT's compatibility with machine-learning algorithms enhances precision of the classification process [12]. Another study using CWT for dynamic cardiorespiratory coupling and aging highlighted a reduction in coupling strength and altered dynamics in the elderly, suggesting age-related changes in heart-respiration interactions [13]. Both papers emphasize the detection of arrhythmias, with the former focusing on SA detection and the latter on aging [12-13]. Lin et al. (2021) significantly advanced sleep medicine by developing a highly accurate algorithm for detecting SA [12]. However, a small sample size and insufficient physiological data restricted deeper analysis [12]. Furthermore, the algorithm was not suitable for patients with irregular ECGs (i.e. cardiovascular complications) [12]. A larger dataset, more comprehensive patient information, and a refined algorithm will broaden applicability, allowing distinction between SA and cardiovascular conditions [12]. Li et al. (2023) found higher heart rate variability indicators in younger participants, suggesting better parasympathetic nervous system function, evident in the LFC/High-Frequency Coupling ratio; however further research is needed to understand these dynamics fully [13].

Using HHT, Liu et al. (2012) achieved enhanced temporal and frequency resolution over FT-based techniques [11]. Their analysis, focused on LFC components, shows a strong negative correlation with AHI, suggesting potential for severity differentiation and treatment assessment [11]. However, this study focuses heavily on LFC components, overlooking High Frequency Coupling, which may occur in obstructive hypoventilation [11]. In another study, the researchers demonstrated HHT's ability to handle non-linear and non-stationary data, offering enhanced accuracy and efficiency of various Structural Health Monitoring scenarios [16].

Wang et al. (2023) addressed the limitations of FT-CPC and improved upon the Wavelet transform-based CPC algorithm [14]. The study, nonetheless, classifies an epoch as an "apnea minute"; this lacks distinction between SA phenotypes [14]. Despite limitations, SST-CPC notably enhanced SA detection accuracy to 83%, showing promise as an effective tool for augmenting traditional SA diagnostics [14].

This review also aims to explore existing literature to identify population bias that may impact the biological conclusions presented. The datasets used in these studies did not have a balanced male: female ratio. Balanced datasets or weighing techniques are important to extract the most accurate conclusions for automated SA detection [17].

V. Conclusion

Our review presents a thorough analysis of current methodologies in CPC for SA detection. By examining an array of advanced signal processing techniques, we delve into the intricacies of how these algorithms interpret the interplay between cardiac and respiratory patterns during sleep. Each method brings its own set of challenges, including the need for larger, balanced datasets, and the risk of bias that may influence the generalizability of findings. Despite these hurdles, the reviewed CPC analysis techniques represent a promising frontier in sleep medicine, laying the groundwork for more nuanced and accessible SA diagnostics.

Conflict of Interest

The authors declare that they have no conflict of interest.

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