# Cardiopulmonary Coupling and its relationship to PSG

## The Technology

Cardiopulmonary Coupling is a patented technology that establishes Sleep Quality from the analysis of the connection between heart rate variability and respiratory volume variability; this coupling will be higher or lower depending on their relative stability. The SleepImage system uses electrocardiogram (ECG) and high precision 3-axis accelerometer data to obtain four data streams, ECG, actigraphy, snoring, and body position using patented algorithms developed and validated by sleep researchers.

The electrocardiogram contains a convenient set of signals for extracting both heart rate variability (HRV) and tidal volume fluctuations. Heart rate variability is calculated from the R-R intervals on the ECG. Respiration activity is derived from the change in amplitude of the QRS complex that is directly related to tidal volume changes with inhalation and exhalation called electrocardiogram-derived respiration or EDR.

The algorithms utilize mathematical and frequency analysis to determine synchronization between modulations of heart rate and respiration and provides visualization of sleep states in an ECG-derived Sleep Spectrogram.
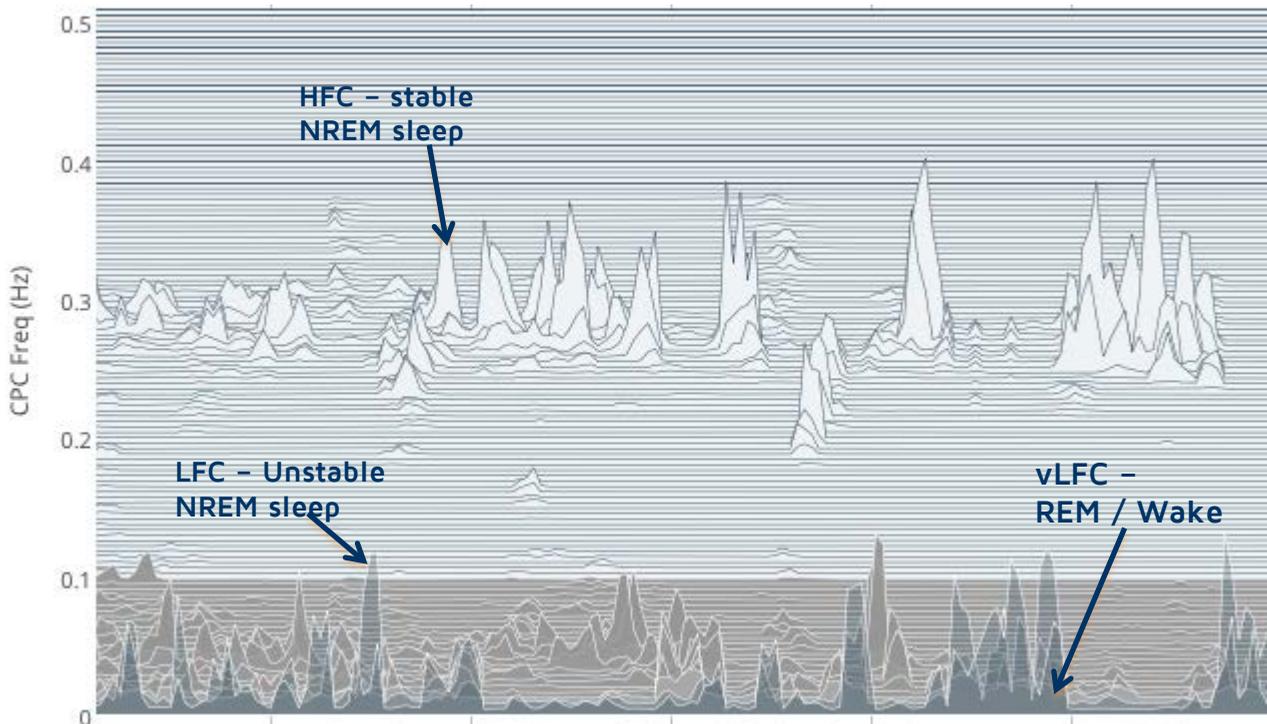


The validation of Cardiopulmonary Coupling (CPC) utilized clinical Polysomnography (PSG) as the standard upon which it was compared. Simultaneous SleepImage and PSG recordings were performed, validated and published and the data shows periods of sleep identified by both systems were correlated. Please go to our research webpage at www.sleepimage.com/research.

The literature historically defined five stages of sleep (1,2,3,4 and REM). Stages 3 and 4 were later combined (by eliminating Stage 4) to represent "deep sleep" or "slow wave sleep" a stage where the brain almost exclusively produces delta waves. Stage 1 happens for a brief period as a person is falling asleep. It is very light sleep as the person is drifting in and out of sleep. Stage 2 was defined as when brain waves slow down with an occasional burst of faster brain waves, eye movement stops. Stage 2 is a transition stage between unstable and stable NREM sleep. The biologic role of NREM sleep is associated with low delta power is unclear.

Restricting such periods produces adverse consequences similar to those of total sleep deprivation including sleepiness and metabolic dysregulation. Electroencephalographic delta frequency activity (usually 0.5-4 Hz) is considered a biomarker of homeostatic sleep drive. Delta power as a proportion of total EEG power is highest during the initial cycles of NREM sleep. It decreases across the biologic night and shows rebound effects after a period of sleep deprivation.

It is important to note that CPC does not rely on the same data streams as PSG. Rather than a dependence on interpretation of primarily EEG morphology, CPC utilizes the physiological changes that occur with sleep via the autonomic nervous system through the "lower" brain centers and networks (including thalamus, hypothalamus, and hippocampus). It integrates information from brain electrical activity, respiration and autonomic drives, capturing the essence of sleep making a "sleep staging" comparison a misnomer. The metrics are independent of absolute EEG amplitudes and thus are not constrained by the "loss" of slow wave sleep with age. The ease of acquisition of the ECG allows Cardiopulmonary Coupling to be assessed from any continuous ECG signal source, be it a formal polysomnogram, a hospital monitor or ambulatory wearable devices recording continuous ECG.

The CPC technology has been validated against thousands of PSG studies and a high level of correlation with PSG sleep power mapping confirmed. The ebb and flow of slow wave power is the accepted marker of sleep drive in humans and in non-human species. Delta power measured from surface EEG correlates with ECG-derived Cardiopulmonary Coupling high-frequency power, further supporting a link between cortical EEG electrical activity and brainstem-related cardiorespiratory functions.

## The Practicality

This correlation between delta power and high-frequency cardiopulmonary coupling is consistent with strong "top-down" modulation of autonomic and cardiorespiratory activity. The Spectrogram below shows the correlation between HFC and normalized delta power (blue line) during simultaneous CPC and PSG data collection.
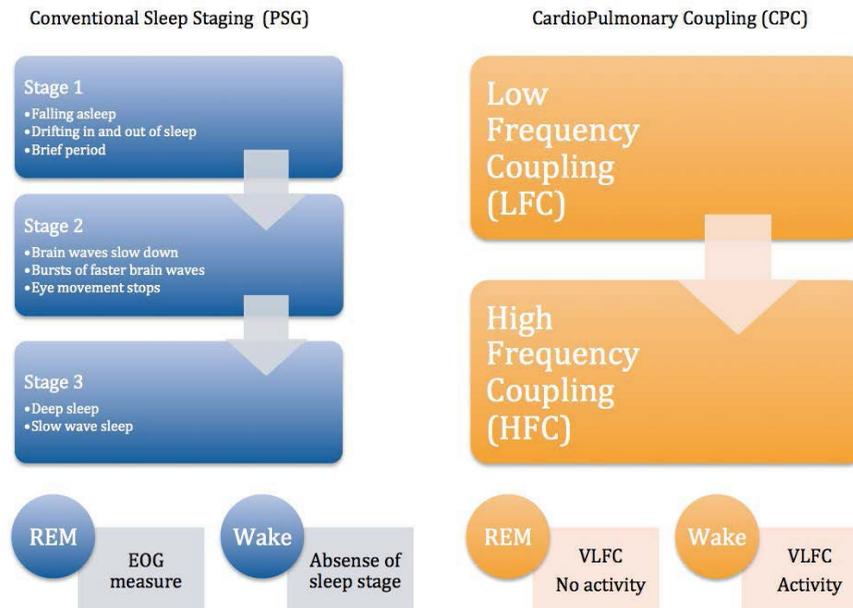
CPC is based on the bimodality of sleep and is represented as High Frequency Coupling (HFC) or stable sleep which only occurs in stable NREM sleep and is thus equivalent to part of Stage 2 and all of Stage 3 when compared to sleep staging and published research has proven the correlation between HFC (stable sleep) and Delta Waves (deep sleep). In this stage, desirable sleep features dominate, including high vagal tone/sinus arrhythmia, blood pressure dipping, high slow wave power and stable breathing. Low Frequency Coupling (LFC) or unstable sleep equates to the part of NREM sleep that is unstable, meaning all of Stage 1 sleep and part of Stage 2. In this stage generally less desirable features dominate, such as cyclic variation in heart rate, absence of blood pressure dipping, tidal volume fluctuations (with sleep apnea of a degree exceeding clinical thresholds) and lower delta power. CPC captures REM and Wake as Very Low Frequency Coupling (vLFC) differentiated by movement – vLFC with activity represents Wake and vLFC without activity represents REM sleep. Fragmented REM sleep takes on LFC characteristics.
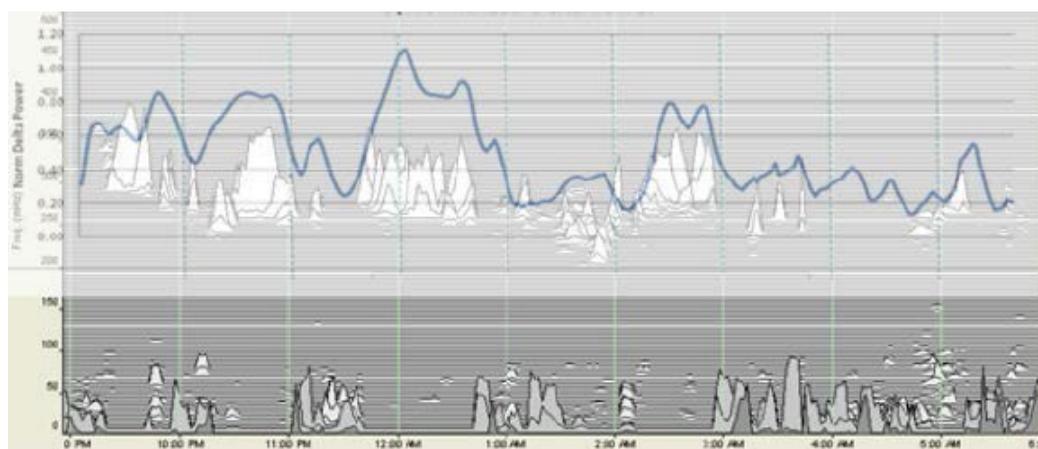


*Dr. Robert Joseph Thomas et al. Relationship between delta power and the electrocardiogram-derived CPC Spectrogram: possible implications for assessing the effectiveness. Sleep Med.2014 Jan; 15(1); 125-131. This shows the correlation between HFC and normalized delta power (blue line) during simultaneous data collection using CPC and PSG.*

These CPC states are separated widely in signal space with no overlap – that is, the boundaries are clean.

So although these two technologies of CPC and PSG come from different directions (ECG vs EEG) the difference between the two does not vary as much as it may seem at first, as shown in the following figure.

Conventional Sleep Staging  (PSG)          CardioPulmonary Coupling (CPC)

**Stage 1**
- Falling asleep
- Drifting in and out of sleep
- Brief period

**Stage 2**
- Brain waves slow down
- Bursts of faster brain waves
- Eye movement stops

**Stage 3**
- Deep sleep
- Slow wave sleep

**REM** — EOG measure          **Wake** — Absense of sleep stage

**Low Frequency Coupling (LFC)**

**High Frequency Coupling (HFC)**

**REM** — VLFC No activity          **Wake** — VLFC Activity

As such, both CPC and PSG are quite capable instruments that assess the same thing but with a different unit of measure. However, there are some important differences as well. In practicality PSG is a test, usually limited to a one-night snapshot to diagnose, while CPC is an objective sleep quality and sleep pathology assessment tool intended to identify and evaluate sleep disorders to inform or drive clinical decisions (aid diagnosis).  Due to the simplicity of collecting data for CPC analysis (only a single-lead ECG is required) it is possible to do multiple tests to see a trend of sleep as a vital sign of good health over time. The CPC Sleep Report therefore provides a new way to look at sleep quality and sleep pathology independent of the conventional electroencephalogram (EEG).

High-frequency (0.1-0.5Hz) coupling (stable sleep) is a biomarker of integrated, stable NREM sleep, which is characterized by stable breathing, high vagal tone, a non-cyclic alternating pattern on the electroencephalogram (generally), high relative delta power, and blood pressure dipping. This state may be considered "effective" NREM sleep. Effective sleep enables the normal functions of sleep, across multiple dimensions (e.g. neuronal network health, metabolic), such that spending periods in this state enables recovery and restoration processes.
Low-frequency (0.01-0.1Hz) coupling (unstable sleep) is a biomarker of integrated unstable NREM, with exactly opposite features: low-frequency tidal volume fluctuations, cyclic variation in heart rate, a cyclic alternating pattern, electroencephalogram low relative delta power and stable (non-dipping) blood pressure. This state may be considered "ineffective" NREM sleep. Ineffective sleep fails to accomplish the normal functions of healthy sleep.

Very-low frequency (0.001-0.01 Hz) coupling (REM/Wake) is seen in the wake state and during healthy REM sleep, the SleepImage system uses accelerometer data (movement) to distinguish between these two states, vLFC with activity represents Wake and vLFC without activity represents REM sleep. Fragmented REM sleep has low-frequency coupling characteristics.

Sleep-fragmenting stimuli increase unstable sleep (low-frequency coupling), and sleep-consolidating stimuli increase stable sleep (high-frequency coupling) as a percentage of sleep, thereby allowing dynamic tracking of sleep physiology and pathology in health and disease.

## The Conclusion

CPC is a practical way to measure sleep disruption or sleep decline with the advantages of access, ease of use, comfort, cost and trending. Unlike PSG, there is no need for a trained technologist to manually interpret the sleep study as it can be interpreted intuitively by the treating clinician, using a "decision-assist" tool that automatically identifies the presence of a sleep disorder to aid clinical evaluation. The SleepImage report is immediately accessible based on data uploaded and saved to a secure cloud-based server. Reports can be compared to evaluate sleep quality, sleep pathology and sleep duration trended over time. The ability to repeatedly perform objective sleep studies in the comfort of the patient's home make evaluation and management of sleep disorders possible for improved patient benefit and treatment efficacy.

The CPC technology is widely applicable in clinical practice and research alike. Poor sleep quality is highly comorbid with many chronic medical conditions such as pain, diabetes, and depression, as well as various cardiovascular, respiratory, neurological and psychological disorders. Undetected and untreated poor sleep quality is a major risk factor for the development and progression of these serious and costly chronic diseases.

Sleep is the 'Vital Sign of Good Health' and SleepImage offers the only FDA-cleared unit of measure for sleep health, the Sleep Quality Index (SQI) that makes tracking sleep health over time both practical and accessible.

For further reference to the science behind CPC, see also:

http://www.sleepimage.com/research

Principles and Practice of Sleep Medicine, (Kryger – Roth – Dement) Sixth Edition, Chapter 166. Cardiopulmonary Coupling Sleep Spectrogram.