

HARVARD RESEARCH UPDATE

NuCalm® is an all-natural anxiolytic clinical solution proven to remediate stress at the midbrain with no significant side effects or required recuperative time. NuCalm was invented by pioneering neuroscientist, Dr. G. Blake Holloway, founder of Solace Lifesciences, Inc., a neuroscience company focused on personalized, evidence-based wellness and performance. NuCalm is the first and only patented system for “balancing and maintaining the health of the human autonomic nervous system.” NuCalm leverages four discreet anxiolytic components into a scientifically sequenced application that creates the following neurophysiologic response:

- Rapid induction of parasympathetic hypnogogic dissociative state
- Sustained, steady parasympathetic dominance throughout the NuCalm experience
- Rapid return to a functional state (motor skills, attention, and full cognition) with no lingering negative post-sedative effects

NuCalm was made commercially available to licensed healthcare practitioners in September 2010, after 8 years of scientific discovery, research, and development. To date, over 400,000 patients across the U.S., Canada, U.K., Europe, Russia, and Australia have experienced NuCalm without a single reported adverse event. Dentists across the globe are using NuCalm to improve the dental experience with exceptional satisfaction rates; 95% of patients state they would use NuCalm again, and over 98% state they would recommend NuCalm to their friends and family.

The anecdotal evidence and reported positive responses to NuCalm have been profound. Many users have likened NuCalm to “meditation in a box.” The meditation analogy is logical considering NuCalm creates parasympathetic nervous system dominance. Most of the parasympathetic innervation (nerve energy) comes from the vagus nerve, which exits the brain and connects to the gastrointestinal tract, respiratory tract, heart, and abdominal organs. Consistent use of NuCalm is proven to help people achieve autonomic nervous system balance, cellular homeostasis, improved stress resiliency, and greater neuromuscular equilibrium. This “reset” resolves the negative impact of stress and positions people for optimal performance.

Quantitatively, Solace Lifesciences, Inc. used numerous neurophysiological biomarkers to validate NuCalm’s anxiolytic response during the arduous U.S. and international patent treaties process.



All of the biomarkers validated a parasympathetic dominant – hypnagogic dissociative state during a NuCalm session:

- Electroencephalogram (EEG at CZ, C3, and C4)
- Quantitative Electroencephalogram (QEEG at 32 sites)
- Neurotransmitter lab panels
- Galvanic Skin Response (GSR)
- Heart Rate Variability (HRV)
- Respiratory Sinus Arrhythmia (RSA)
- Blood Volume Pulse (BVP – vasoconstriction)
- SCP (Slow Cortical Response – DC – brain activity and cerebral blood flow)
- Alpha-Theta Crossover – % time Alpha amplitude over Theta amplitude

In October 2012, Solace Lifesciences, Inc. began collaborating with statistical biophysicists Dr. Chung-Kang Peng and Dr. Yanhui Liu to study the positive impact NuCalm has on autonomic nervous system balance and restorative sleep.

Dr. Peng is one of the world's preeminent experts on Heart Rate Variability (HRV). His research has been cited over 23,000 times in medical journals. Dr. Peng is the Co-Director of the Rey Institute for Nonlinear Dynamics in Medicine at the Beth Israel Deaconess Medical Center and Associate Professor of Medicine at Harvard Medical School. Dr. Peng and his colleagues have proven definitively a method to identify stages of sleep including breath disturbed sleep using single channel ECG-based spectrogram and an algorithm developed by Dr. Norden Huang. The Hilbert-Huang Transform (HHT) was developed for NASA and is used to decompose a signal into intrinsic mode functions to obtain instantaneous frequency data.

“From our preliminary study of a small group of volunteers using NuCalm, we observed that these subjects experience a rapid decrease in heart rate and respiration rate while exhibiting an increase in vagal tone. These physiological biomarkers are consistent with deep meditation and illustrative of the rapid onset of parasympathetic nervous system dominance created by NuCalm. Our preliminary results indicate that the NuCalm system could be a powerful tool for stress intervention and sleep quality improvement.”

— Chung-Kang Peng, Ph.D., Co-Director, Margret and H.A. Rey Institute for Nonlinear Dynamics in Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School



Dr. Peng and Dr. Huang are co-directors of The Center for Dynamical Biomarkers and Translational Medicine with the following research focus:

- Building mathematical models of multi-scale structure properties in biomedical signals
- Cerebral auto-regulation dynamics in stroke patients
- Probing the underlying characteristics of biological rhythms in multimodality approaches
- Investigating the mechanisms of sleep homeostasis
- Innovative medical imaging processing and analysis tools
- Identifying dynamical biomarkers to predict the success of the atrial fibrillation ablation procedure
- Large-scale population study of long-term blood pressure monitoring
- Dynamical biomarker analysis of cardiovascular diseases
- Developing a fall-risk evaluation and balance stability enhancement system by measuring noninvasive physiological signals

Dr. Peng and professor/psychiatrist Dr. Albert Yang co-developed an information-based categorization algorithm while Dr. Peng was a post-doctorate fellow at Harvard. The method was based on an idea Dr. Peng developed when he was a physics graduate student, in which he combined the concepts of Shannon Entropy Theory and statistical physics. Dr. Yang was able to effectively apply the method to distinguish heart beat patterns in health and various diseases. Later, the two applied the algorithm to study a major authorship debate in Chinese literature, and were able to demonstrate that “The Dream of the Red Chamber” (a famous 18th century Chinese novel) was written by two authors. When showing this result to their colleagues at Harvard, Dr. Goldberger suggested that the two examine the plays by William Shakespeare. Their method was able to identify that the play “Edward III” was written by Christopher Marlowe, not William Shakespeare. For their contribution, they were awarded the 2003 Hoffman Prize: <http://www.marlowe-society.org/reading/info/hoffmanwinners.html>. Dr. Peng and Dr. Albert Yang subsequently used this method to study DNA sequences.

Dr. Yanhui Liu founded DynaDx Corporation in 2005 as a technology incubator. DynaDx develops technologies that leverage the advances in dynamical signal analysis to improve clinical diagnosis and prediction ability. The company's products are based on dynamical analysis of physiologic signals, including ECG, EEG, blood pressure, respiratory, and neuromuscular signals. DynaDX created a heart rate monitor - single lead ECG EZ Sleep device that uses the Huang algorithm to accurately measure Heart Rate, Respiration Rate, and Respiratory Sinus Arrhythmia (RSA). RSA is a sensitive and accurate measure of vagal tonality and an indicator of parasympathetic nervous system dominance. The vagus nerve serves as a bridge between the brain and the heart and vagal tone measures autonomic nervous system health. This measurement opens a window to one of the most powerful regulatory systems in the body - viscera and the endocrine system.

The figures below show NuCalm subject data using the ECG EZ Sleep device. The 30-minute NuCalm session is outlined by the vertical lines. The subject experienced a rapid decrease in heart rate and respiration rate while exhibiting an increase in vagal tonality. These biomarkers are consistent with deep meditation and indicate the rapid, predictable onset of parasympathetic nervous system dominance created by NuCalm.

Figure 1: Heart Rate

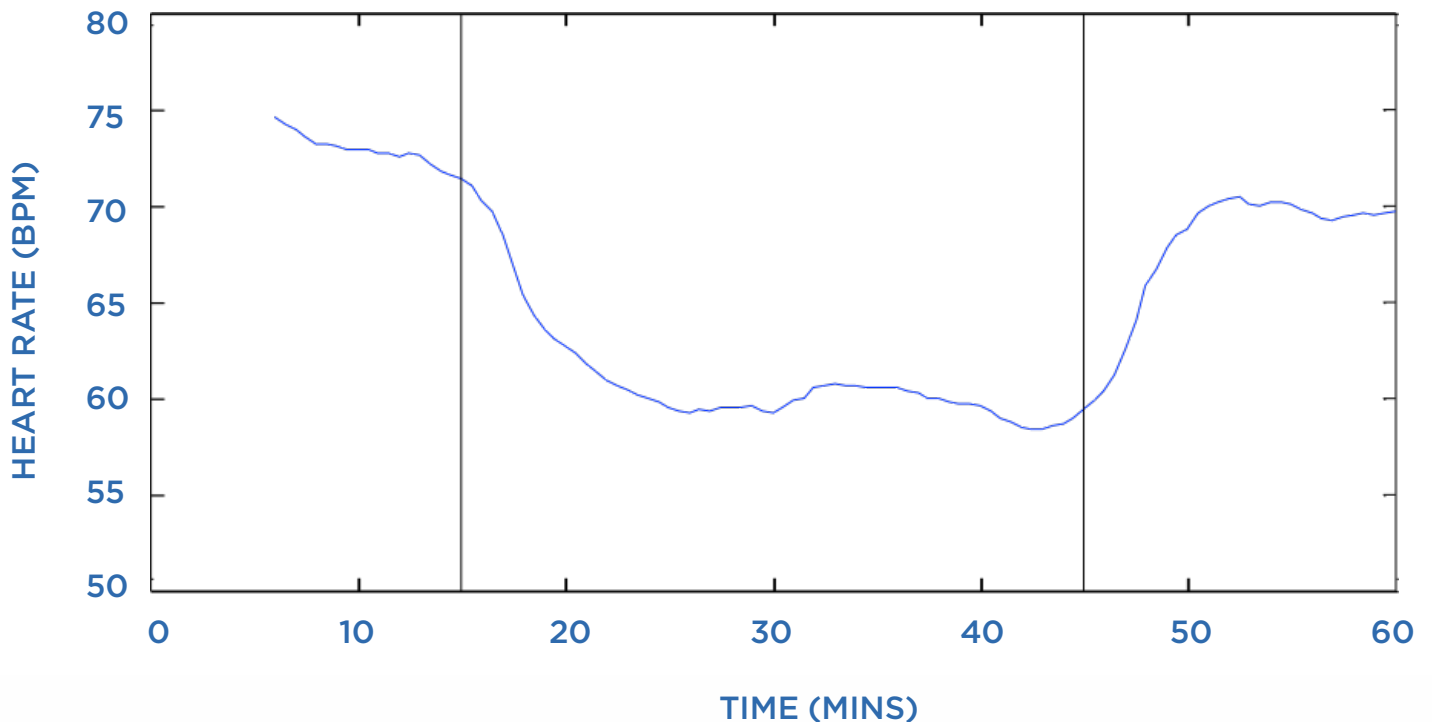


Figure 2: Respiration Rate

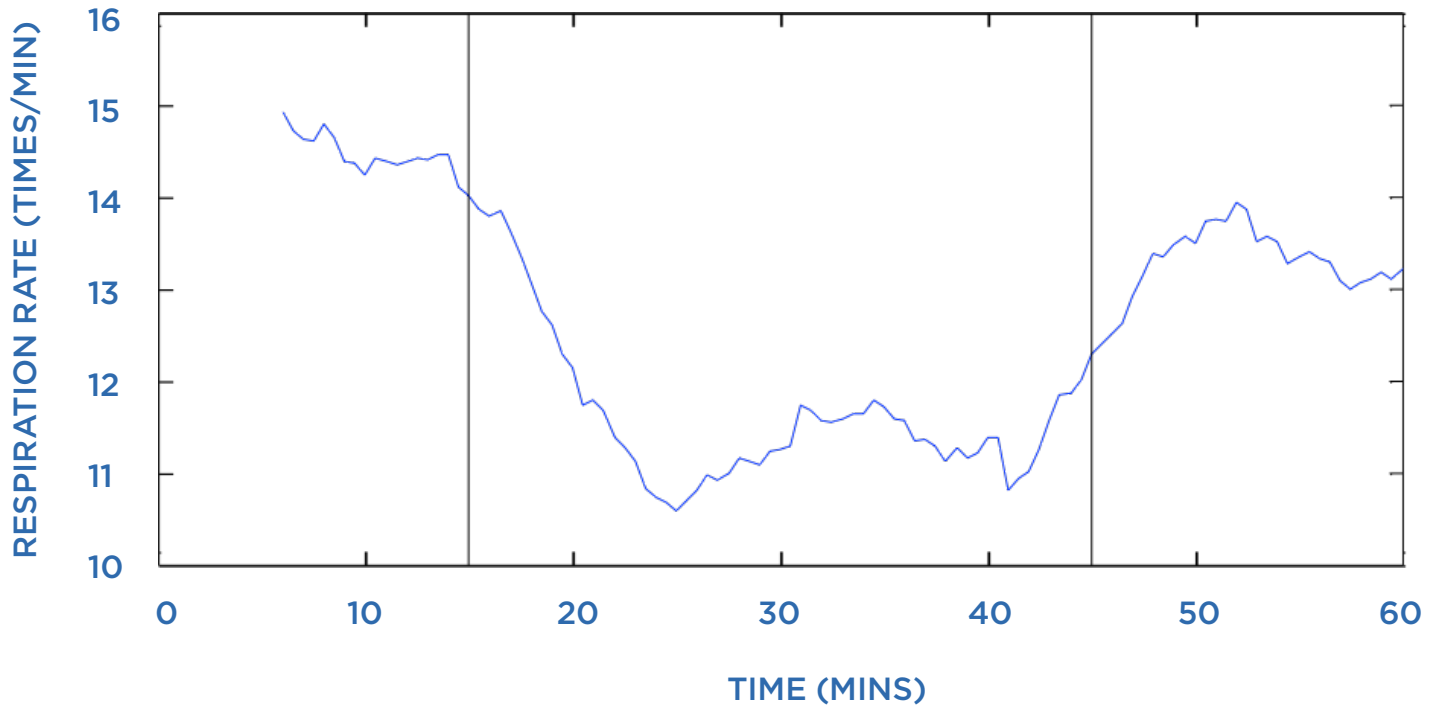
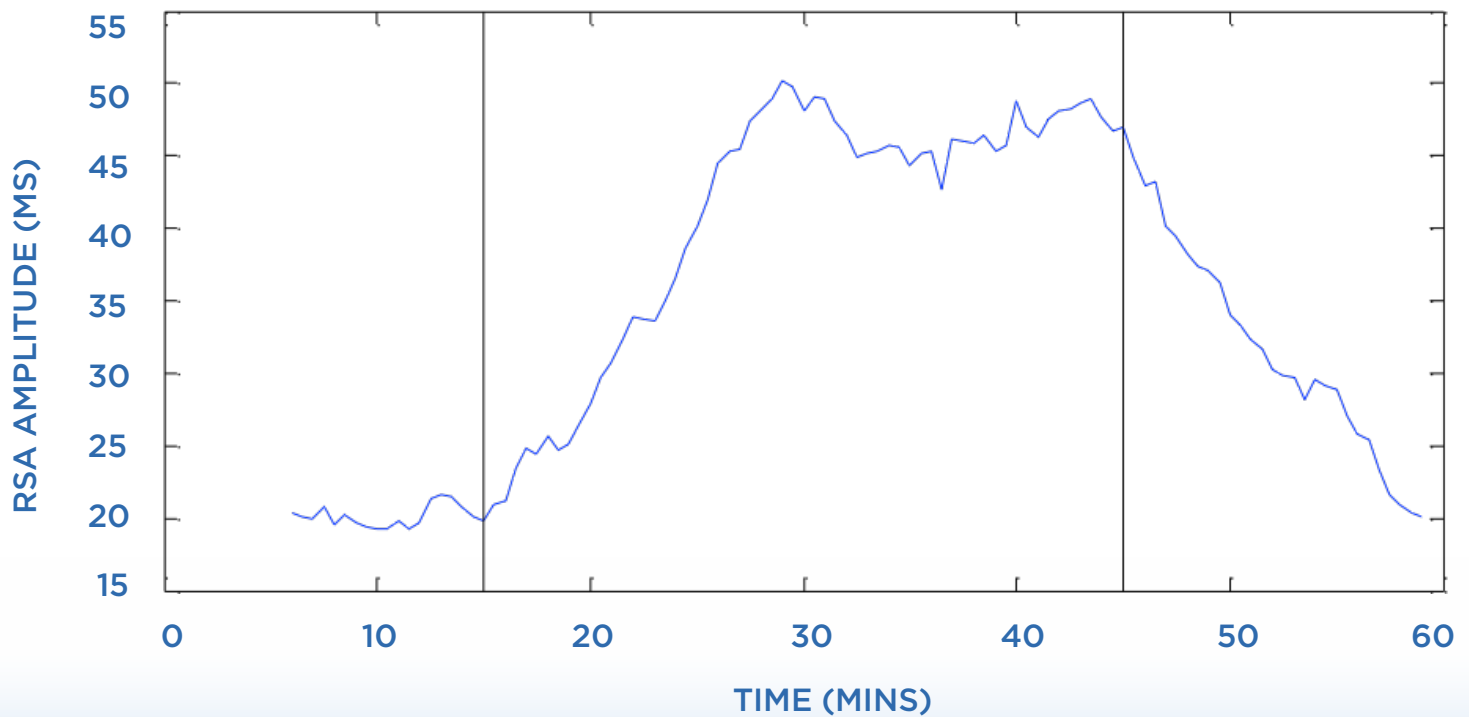


Figure 3: RSA Amplitude





NuCalm and Sleep Architecture Enhancement

Inadequate sleep afflicts over 50 million people in the United States, contributing to reduced cognitive function and psychiatric disorders. The ubiquitous problem caused by the hyper-stressed culture in the U.S. is erratic sleep stability. People with poor sleep quality are 1.97 to 6.3 times more likely to develop anxiety disorders and 4.0 times more likely to develop psychiatric disorders in general (Taylor, Lichstein, & Durrence, 2003). Anxiety disorders are estimated to affect 25% of the population over their lifetime and are associated with significant personal, social, and economic costs. Sleep fragmentation of any cause is disruptive to the rejuvenating value of sleep. Good sleep promotes good health and prevents the onset of disease. Conceptually, the concomitant use of NuCalm (cranial electrical stimulation, neuroacoustic entrainment, and light-blocking eye masks on an individual that has ingested the proprietary NuCalm dietary supplements) should enhance sleep architecture.

The Standard American Diet (SAD) is frequently deficient in the macronutrients that the brain requires to produce the neurotransmitters necessary for stable sleep. At present, there are few non-pharmacological enhancements available to the general public. Pharmacological enhancements are not optimal due to side effects and the fact that they do not restore normal biological sleep architecture.

Solace Lifesciences, Inc. is collaborating with Dr. Peng and Dr. Liu to develop and study a model for personalized, evidence-based, wellness and performance using the ECG EZ Sleep device for quantitative measurements and diagnostics and NuCalm as the foundation for a wellness platform. Dr. Peng has developed a measure (index) of the complexity for people in compromised health conditions, such as hypertension and obesity. DynaDx, under the guidance of Dr. Liu, started an IRB approved study at the prestigious National Taiwan University Hospital (NTUH) in January 2012. Enrollment of healthy subjects reached over 850 this June. The objective of this study is to establish an index for healthy people. Research efforts continue to correlate the multitude of time and frequency domain analysis of DynaDx's data capture tool.

Professor Albert Yang, a world-renowned research scientist and psychiatrist at Taipei Veterans General Hospital and former collaborator with Dr. Peng, is exploring a research study to validate the impact NuCalm can have on insomnia and improving sleep quality.