

THE UTILITY OF HEART RATE VARIABILITY IN AVIATION AND SPACE MEDICINE



Corresponding Author

Dr Karen Lindsay BSc (Hons) Biomedical Science, MbChB, FRACP

Department of Clinical Immunology and Allergy

Level 6 Support Building

Auckland City Hospital

Grafton Road, Auckland, New Zealand

Email: klindsay@adhb.govt.nz

Co-Author

Erik Van den Top MHSC (University of Auckland)

Transformative Insights Limited

27 Ewen Alison Avenue

Devonport, Auckland 0624, New Zealand

Email: erik@transformative-insight.com

KEYWORDS:

ANS: Autonomic nervous system; PNS: Parasympathetic nervous system; SNS: Sympathetic nervous system; RR: Time between R-R intervals (ms) on an ECG lead; RSA: Respiratory sinus arrhythmia is heart rate variability in synchrony with respiration, by which the R-R interval on an ECG is shortened during inspiration and prolonged during expiration; SDNN: Standard deviation of all normal-to-normal RR intervals (ms); RMSSD: Root Mean Square of successive RR interval differences (ms); pNN50: The percentage of intervals > 50 ms different from preceding interval; ULF-HRV: Magnitude of variance in the frequency band 0.15-0.40 ; LF-HRV: Magnitude of variance in the frequency band 0.04–0.15 Hz; HF-HRV: Magnitude of variance in the frequency band 0.15-0.40; LF/HF: ratio Low Frequency (LFn) (ms²)/ High Frequency (HF_n) (ms²)

ABSTRACT

Heart rate variability, with modern technology detects the differences between each electro cardiac signal of the heartbeat, and is being utilized across a broad number of fields in aviation and space medicine, such as simulation training, assessment of performance and improvement in safety and wellbeing and has potential in the prediction of incapacitation in Civil Aviation Medicine, from both physical and mental health problems, and monitoring of astronauts in space flight. HRV has seen increasing utility across aviation and aerospace medicine but also has potential as a marker of -chronological aging, stress, cognitive load, recovery and optimal performance. Data needs to be gathered on the population being studied at baseline, and under physiological stress and recovery in the long term and potentially in the occupational role. Aviation Medical examiners need to be skilled at critical analysis of HRV data in predicting incapacity particularly in the aging pilot where there may be many cofounders. HRV biofeedback may enhance aviation medical wellbeing interventions. Aviation Medical Examiners would benefit from understanding the current use and potential of Heart rate variability data.

INTRODUCTION

What is heart rate variability

Heart rate variability (HRV) simply put, is a measure of the variation in time between heartbeats (1). The single lead electrocardiogram (ECG) provides information about differences in RR interval length in the QRS complex. Heart rate is determined by intrinsic activity of the sinoatrial node, supplemented by innervation from the vagus nerve which reflects the activity of the parasympathetic part of the autonomic nervous system (ANS). The sympathetic nervous system (SNS) part of the ANS leads to a reduction in HRV through the release of adrenaline and noradrenaline in the blood stream, which impact the sinoatrial node and heart muscle over a period of minutes, while the two (vagal) nerves of the parasympathetic part (PNS) leads to an increase in HRV through the release of acetylcholine from nerves, within seconds (2). HRV is also influenced by respiration. On inspiration the SNS dominates, and on expiration the PNS dominates, creating a respiratory sinus arrhythmia (RSA). At rest and during mild exertion,

the parasympathetic (vagal) control outweighs the sympathetic effect. In the paradigm of homeostasis of a healthy person, the interaction of the SNS and PNS leads to changes in heart rate variability (3).

A shift in paradigm to systems and chaos theory meant that HRV became understood as an emergent property of interdependent regulatory systems that help humans' adaptation to environmental and psychological challenges (2). Up to 80% of vagal fibres are afferent, providing vital information to the brain about the state of the visceral organs. HRV is a window into the synchronization of brain and heart oscillations (4), and low frequency diurnal variation reflects hypothalamic and endocrine function. Figure 1 shows the broad range of function of the ANS (5). The number and variety of HRV studies has increased exponentially into many different research areas and HRV is increasingly being used alongside Artificial intelligence (AI) (6), and in Occupational Medicine, to evaluate the internal physiological response to changes in temperature, air pressure, oxygenation and pollution and workload (7, 8).

Sympathetic division	Organ effected	Parasympathetic Division
-Pupils: dilate		-Pupils: constrict
-Saliva: inhibited		-Salivation
-Airways: dilate		-Airways: constrict
-Heart rate: increases		-Heart rate: slows
-Stomach: inhibits digestion		-Stomach: digests
-Liver: releases glucose		-----
-Intestines: inhibit digestion		-Intestines: digest
-Kidneys: release adrenaline		-----
-Bladder: relaxes		-Bladder: constricts
-Reproductive system: decreases blood flow		-Reproductive system: increases blood flow

Figure 1 shows the functions of the autonomic nervous system (5).

WHAT INFORMATION CAN BE DISCOVERED FROM HRV DATA?

HRV data collection through technology that is affordable, non-invasive and pain free making it readily accessible as wrist watches, rings and other wearables which accurately measure HRV (9) HRV may have clinical utility, for example HRV can be used to

diagnose early onset of sepsis e.g. in SARS- Covid-19 infection, as well as track patients progress and recovery (10, 11). There are four domains of analysis in HRV. Time domain, frequency domain, power domain and non-linear methods (2). Figure 2 shows the different outputs that are possible HRV analysis (8). Table 1 shows the metrics used to express HRV.

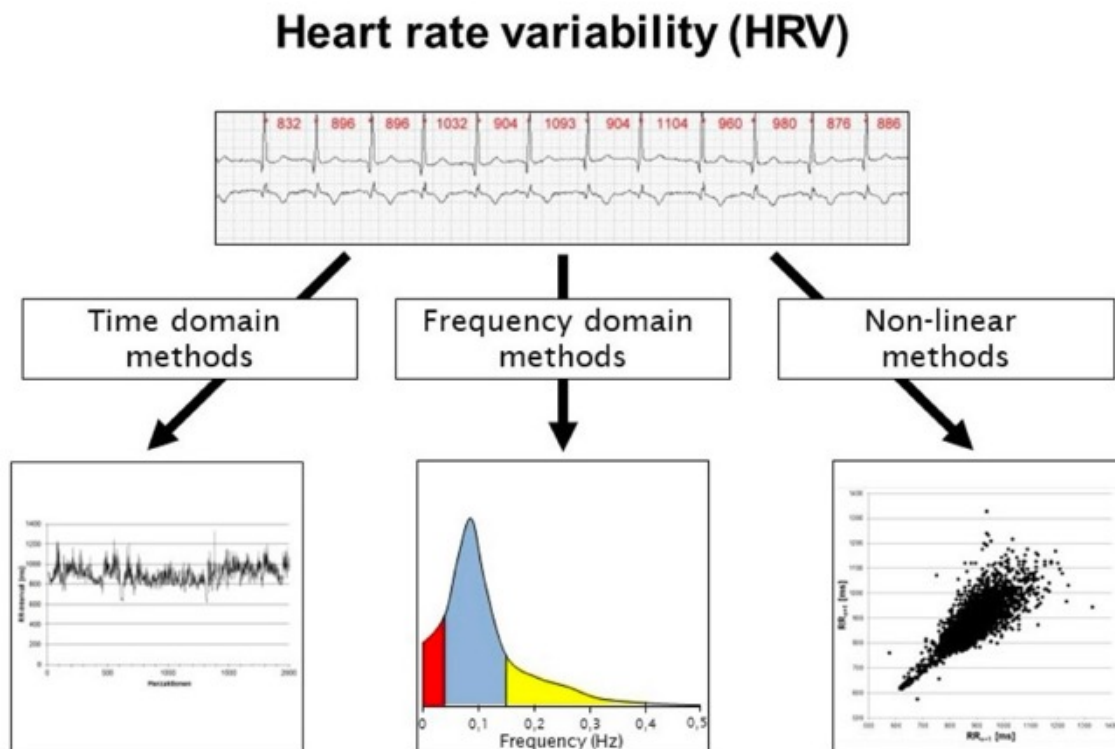


Figure 2 shows the different outputs that are possible HRV analysis (8).

Time Domain		Unit	Physiological equivalent	Meaning	High level	Low level
	SSDN	Millisecond (ms)	Total heart rate variability correlated with ANS activities. All the cyclical influences of physiological processes on the heart	Standard deviation of the normal-to-normal interval	Physiologic resilience against stress	Risk of coronary artery disease. Hypertension, diabetes Depression Cognitive decline (7)
	RMSSD	ms	Parasympathetic innervation of the heart Free from respiratory influences	Root mean square of successive differences between normal heartbeats	Good for short term assessment of HRV in-flight	
	pNN50	%	Vagal tone	Percentage of successive normal sinus RR intervals more than 50 ms		
Frequency Domain	LH	(0.04 to 0.15 Hz) Ms2	PNS and SNS combined	Increased sympathetic activity during mental stress and exercise.		
	HF “The respiratory band”	(0.15 to 0.4 Hz) Ms2	PNS	High frequency variations in HRV		Higher stress, panic, anxiety or worry.
	LF/HF ratio		Balance between SNS and PNS activity		SNS dominance	PNS dominance
	Very Low Frequency Range	0.0033 to 0.04 Hz	Long-term regulation mechanisms, thermoregulation and hormonal mechanisms Astronaut exposure to Space weather (magnetic)			
	Ultra-low Frequency It can be only assessed with 24 h recording	below 0.0033 Hz. Ms2	Circadian oscillations, core body temperature.			

Table 1 Metrics used in HRV

Certain dimensions of the HRV reflect vagal nerve mediated parasympathetic tone. Short measurements over a few minutes show the respiratory cycle and baroreceptor reflexes influence on HRV, which are hence high frequency variations (HF). Low frequency variations (LF) reflect SNS and PNS combined. Non-linear analyses such as the Poincaré plot depict variations in vagal tone at baseline and under stress situations, but the most evidence is for the physiological equivalent of vagal tone (RMSSD, and HF-HRV) (12). The RMSSD is the most widely used measure of HRV and is likely to have the most practical utility in aviation, as it best reflects the domains of interest in aviation and can be accurately checked also over time through nighttime measurements using wearable devices to complement in-flight measurement of HRV (9). This monitoring may signal both to the pilots themselves and the aviation medical examiner a (chronic) undesirable change in HRV trends that may show impending reasons for incapacitation for example cardiovascular disease.

OBSERVATIONS OF HEART RATE VARIABILITY IN CONDITIONS RELEVANT TO MEDICAL EXAMINERS.

Cardiovascular risk

International Civil Aviation Authority regulations state prior to allowing a pilot to fly, they must have a medical certificate. Aeromedical assessment of cardiovascular and cerebrovascular risk is based on history examination and judicious requesting of specialist assessment and tests, to aid in the prediction of human factors that could cause incapacitation in flight. HRV is an established predictor of cardiovascular mortality in those with and without known coronary artery disease (13) (14) (15)). (16). HRV is also reduced with hypertension, diabetes, and ischaemic heart disease in occupational studies (8). AI supported databases use HRV to develop predictive models in cardiovascular disease (6).

COGNITION AND AGEING

The autonomic nervous system shows age-related changes linked to lifelong patterns of behavior, and physiological responses to stressors, all being reflected in the lowering of vagal tone, the long-term consequence of stress known as 'allostatic load', measurable by reduced HRV (5). Autonomic dysfunction has been shown to be associated with the development of different age-related diseases, including ischemic stroke, cardiovascular disease, and inflammatory diseases which accumulate with the aging aviator, in a non-chronological manner. The vagus nerve parasympathetic nervous system, inclusive of acetylcholine receptors, downregulates inflammation the so called neuroinflammatory reflex which has been investigated using vagal nerve stimulation to treat diseases such as rheumatoid arthritis (17). In a systematic review of longitudinal studies, reduced HRV indicates poorer cognition, cerebral blood flow and working memory over time, and authors suggest HRV can be a biomarker of cognition over time. (16). HRV

therefore has potential to predict inflammatory non-chronological age-related diseases in pilots relevant to the aviation medical examiner.

MENTAL HEALTH

Pilots often withhold mental health symptoms like suicidality (18). HRV has been extensively studied in depression, posttraumatic stress disorder, stress reactivity, including its use in biofeedback for training resilience (6, 19-21). Studies have found a significant association between PTSD and reduced levels of both high-frequency HRV (HF-HRV), which is highly correlated with respiratory sinus arrhythmia (RSA), and low frequency HRV (LF-HRV) (22, 23). HRV is also a dynamic window on brain function and has been shown in studies to be reduced in threat or stress responses, associated with reduced cerebral blood flow. Higher HRV is associated with better emotional regulation (24). Dr Stephen Porges' lifelong study of HRV led him to propose that repeated stressors can lead to down-regulation of cardiac vagal tone and chronic up-regulation of sympathetic activity (hyperarousal) at rest, thus linking anxiety and HRV and trauma, providing a valuable current model for measuring therapeutic interventions for trauma (so called Polyvagal Theory)(25).

HRV STUDIES IN AVIATORS

Research on the complex factors affecting psychophysical state in flight may lead to measures that can reduce the contribution of human error to aviation accidents. Reduced HRV was found in those with known factors affecting HRV (high BMI, older age and increased difficulty of performance) but not CO₂ levels. They observed there are complex relationships with aviators and the stress of performance, in some instance stress indicated better performance(26). In-flight HRV measurement using three 60 second periods of R-R measurements from a Faros E-motion 3 lead chest ECG, HRV showed significant quantitative differences in performance in virtual vs real flight tests, but qualitatively the changes in HRV were the same in distinct stages of a flight, e.g., take-off, downwind, landing (27).

HRV is the most studied physiological measure for stress evaluation in military reservists, guardsmen and first responders in the United States and even indicates post-traumatic growth (19). HRV (HF-HRV) is also an objective measure of the stress response during decision making and mental workload in simulated and real flights in pilots (28) for a comprehensive narrative review. HRV can be incorporated into the cockpit environment for measurement. HRV data from pilots in flight simulations, showed subjective data such as reflective questionnaires (NASA-Task load index) alone, are limited but in flight HRV measurement was much more reliable of workload intensity and predicted the propensity to error (29). Stress lowered HRV, in helicopter pilot training when switching from analogue to digital visual presentations of the flight and navigation data (30). HRV adds value to the assessment of proficiency in aviation simulation training (31).

HRV analysis can provide inflight physiological data on the startle, surprise responses which causes mental incapacitation. Also in simulations training, providing biofeedback can aid in preparing pilots for the unexpected and better enable pilots to overcome the internal physiological responses that can create cognitive impairment, tunnelling, and lock down (32).

There may be blended states such as 'flow' states of ideal and peak performance, for example being at the peak of a U-shaped curve may be the ideal state of balance between SNS and PNS (33). Likewise HRV state may also be optimal performance and recovery from fighter pilot's stress (34).

Whilst studies have yet to link long term mental health outcome measures and baseline HRV measurement in pilots, intervention on training using HRV biofeedback to enhance resilience and wellbeing of HRV and as an outcome in pilots has shown promise (35, 36). Also HRV as biofeedback can be an adjunct to the Aviation Medical exam, as a motivational intervention as part of lifestyle precision medicine which can be tailored to a wide variety of individual medical conditions or occupational environments (37).

HRV IN MILITARY AVIATION

In the future, individualized biofeedback in military aviation training may form part of the future evolution of human-machine cooperation and add value in the investigation of physiological episodes (PE), contributing to military aviation near-misses and accidents (38). Physiological monitoring in the military includes respiratory oxygen gas levels, functional Near infra-red Spectrophotometry (fNIRS) as a marker of cerebral blood flow (CBF), EEG and ECG, some of which are challenging to integrate into military clothing and cockpits. HRV is being used amongst several other modalities, in several countries' air forces, for fighter pilot simulator training to measure stress and cognitive load, but also the effectiveness of recovery activity (39). Vagal tone (HRV) decreases in Hyperoxia, hypercapnia, and reduces in Hypobaric and hypoxic tasks, early in gravitational loss of consciousness (G-LOC), whole body vibration, heat stress, and sleep deprivation. HRV can be increased by low frequency whole body vibration. A HRV measurement index may be able to measure the cognitive task load under simulated conditions in military training and can differentiate between successful and failed maneuvers (40). HRV is being used to quantitatively assess cognitive load during simulated flight conditions to assess and increase the safety of cadet training (41).

OUTER SPACE AND MICROGRAVITY

HRV was the chosen outcome measure to study aging on the international space station when the surprising anti-aging effect of long-term space travel on nematodes in space was noted. HRV was associated with diurnal rhythms, and VLF-HRV the effect of geomagnetic 'space weather' in astronauts (42). HRV measurement could be used alongside artificial intelligence to enhance remote monitoring of wellbeing in space (43).

The following are drawn from guidelines regarding HRV research

1. HRV measurement is sensitive to different methodological aspects, which hinders direct comparison between studies.
2. Different outcomes require different duration of measurement e.g., SSDN needs several hours of recording for a correct analysis, very low and ultra-low frequency time outcomes may require 24 hours of measurement.
3. Any chosen outcome measure should be one with a strong physiological correlate such as RMSSD of vagal tone.
4. HRV data is rarely of value alone and must usually be supplemented by other questionnaires or physiological data when looking at the outcome being measured.
5. HRV experiments are usually underpowered to find effects sizes, so it is important to ensure researchers have powered a study correctly when planning HRV research.
6. Normal HRV values are affected by the rate of respiration which should ideally be between 9 and 24 cycles per minute and the same across subjects in particular studies. The respiratory rate should be recorded.
7. Movement artifact, whereby muscular discharges interfere with ECG measurement need to be removed prior to analysis. RR interval should ideally be measured from the observation of raw ECG data. Nocturnal measurement methods to measure resting HRV is preferred and have been validated (9).
8. The analysis of HRV data has been made very accessible through a free popular software, Kubios (44) but this can miss data, favouring raw data analysis.
9. Ideally the raw data analyst should be blinded to the intervention to prevent the introduction of bias.
10. When studying interventions on in-flight performance challenges, habituation is a recognized phenomenon, so variation in the challenge being investigated is suggested.
11. Normal measurements for Healthy adults have been published (45) but conclusions based on HRV research should ideally be from normative data in the population being studied i.e., pilots (46).
12. There are revealed large inter-personal variation for the majority of HRV measures. Making the participant their own control with at least 5 minutes resting data is suggested (3, 8).
13. As a novel environment further studies and validation of the impact of space travel on human physiology and HRV are warranted (43).

CONCLUSION

HRV has seen increasing utility across aviation and aerospace medicine but also has potential as a marker of both mental and physical disease, non-chronological aging, stress, cognitive load, recovery and optimal performance. Data needs to be gathered on the population being studied at baseline, and under physiological stress and recovery in the long term and potentially in the occupational role. Aviation Medical examiners need to be skilled at critical analysis of

HRV data in predicting incapacity particularly in the aging pilot where there may be many cofounders. HRV biofeedback may enhance aviation medical wellbeing interventions. The study of HRV and its utility as biofeedback and as a potential window on autonomic neuroplasticity is likely to enhance future developments in pilot training, mitigating the impact of occupational workload, and potentially retrospective investigation of aviation accidents.

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