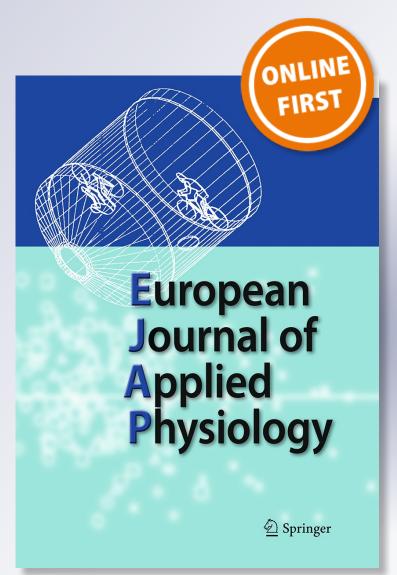
Heart rate variability and critical flicker fusion frequency changes during and after parachute jumping in experienced skydivers

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ORIGINAL ARTICLE

Heart rate variability and critical flicker fusion frequency changes during and after parachute jumping in experienced skydivers

M. Cavalade · V. Papadopoulou · S. Theunissen · C. Balestra

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Abstract

Purpose The purpose of this study was (1) to further explore the heart rate dynamics and assess a potential cardiovascular risk in response to 4000 m jumps in experienced skydivers; (2) to assess whether there is an impact of such jumps on skydivers' cortical arousal or not, which may impact their decision making processes.

Method 18 experienced skydivers performed successive jumps from a plane at 4000 m of height. Heart rate dynamics and cortical arousal were assessed by the use of heart rate variability and Critical Flicker Fusion Frequency (CFFF), respectively.

Results CFFF did not differ between the three measurement time points (p > 0.05). Mean heart rate increased during the jump (p < 0.001) and came back to pre-jump values after the jump (p < 0.001). Percentage of the differences of successive NN intervals greater than 50 ms (pNN50) decreased during the jump (p < 0.001) and kept lower values after the jump compared to pre-jump (p < 0.05). High-frequency power (HF) did not differ during the jump

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(p > 0.05) but decreased after the jump compared to both pre-jump (p < 0.01) and jump (p < 0.05). Sample entropy decreased during the jump (p < 0.001) and came back to pre-jump values after the jump (p > 0.05).

Conclusion These results confirm a vagal input reduction associated with a rise of the sympathetic tone during the jump and suggests that the experienced skydiver is not exposed to a high cardiovascular risk. This study also shows that environmental stresses induced by free fall could not hamper the perceptual vigilance of experienced skydivers.

Keywords Human · Free fall · Non-linear analysis · Fractal · Adverse effects · Environmental stress · Autonomic nervous system · Physiology

Abbreviations

ANOVA	Analysis of variance
ANS	Autonomic nervous system
CFFF	Critical flicker fusion frequency
ECG	Electrocardiogram
EEG	Electroencephalogram
FrD	Fractal dimension
HPA	Hypothalamic-pituitary-adrenal
LED	Light-emitting diode
LF	Low-frequency power
HF	High-frequency power
HR	Heart rate
HRV	Heart rate variability
pNN50	Percentage of the differences of successive NN
	intervals greater than 50 ms
RMSSD	Square root of the mean squared differences
	between successive RR intervals
RSA	Respiratory sinusal arythmia
SampEn	Sample entropy

- SD1 Standard deviation of the points perpendicular to the line-of-identity of the Poincaré plot
- SD2 Standard deviation along the line-of-identity of the Poincaré plot

Introduction

The way that humans can cope with extreme environmental stressors is of great interest to understand some pathologies and also to adapt our approach to the elderly (Mogford et al. 2002; Wagner et al. 1974; Analitis et al. 2008). Parachute jumping is considered as a "real-world acute emotional stress" or "life-threatening" event (Mujica-Parodi et al. 2009a, b; Dikecligil and Mujica-Parodi 2010) and thus commonly used as a model to assess the physiological mechanisms involved in the acute stress response (Dikecligil and Mujica-Parodi 2010; Hare et al. 2013). In particular, free fall has been studied in beginners with the scope of understanding psychological rather than environmental stress (Chatterton et al. 1997; Dikecligil and Mujica-Parodi 2010; Roth et al. 1996; Hare et al. 2013; Taverniers et al. 2011; Cavenett and Nixon 2006). During parachute jumping, it seems well admitted that the steady-state response to the stress exposure is an increase in heart rate (HR) (Shane and Slinde 1968; Reid et al. 1971; Schedlowski and Tewes 1992; Roth et al. 1996). Nevertheless, the mechanisms involved are influenced by many factors and are as such difficult to study. The cardiovascular system is indeed challenged by various combinations of the direct effects of physical exercise, posture, hypoxia, cold, respiration, mental load personality and anxiety found in skydiving (Mullen et al. 1997; Niebauer and Cooke 1996; Hultgren 1992; Granberg 1991; Grossman 1983; Gorman and Sloan 2000; Valentini and Parati 2009).

Hare et al. (2013) showed recently that the anxiety state is higher before a skydive in novice, relative to experienced jumpers. Interestingly, studies which have investigated HR have observed increases in heart rate in both novice and experienced jumpers (Roth et al. 1996; Allison et al. 2012; Leach 2008) which suggests that the increase in HR in experienced jumpers is not solely induced by psychological stress. In particular, at 4000 m of height, skydivers are exposed to acute hypoxia which by itself is known to induce autonomic shifts in cardiovascular regulation by the Autonomic Nervous System (ANS) (Liu et al. 2001; Chen et al. 2008; Zhang et al. 2014; Buchheit et al. 2004). In the past decades non-invasive techniques based on heart rate variability (HRV) have been used as markers of autonomic modulation of the heart (Stein et al. 1994; van Ravenswaaij-Arts et al. 1993; Sztajzel 2004). A few studies which have addressed the clinical significance of linear and non-linear analysis of HRV tell us about a potential cardiovascular risk associated with the dominance of one of the branches of the ANS (Goseki et al. 1994; Krstacic et al. 2007; Kleiger et al. 1991). It is then paramount to further explore this ANS modulation in experienced, rather than novice, skydivers to enhance our understanding of the cardiovascular dynamics to skydiving.

In 1996, standards of measurement, physiological interpretation and clinical use of HRV were defined and established by the Task Force of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology (NASPE) (Task Force 1996). Time domain indices (Cowan 1995; Kleiger et al. 1992), geometric measures (Cripps et al. 1991; Hnatkova et al. 1995) and frequency domain indices (Malliani et al. 1991, 1994) constitute nowadays the standard clinically used parameters of HRV. Nevertheless, the heart rate signal has recently been demonstrated to behave as a non-linear dynamical system in different conditions (Lewis and Short 2007; Goldberger 2006). Therefore, it is appropriate to also apply non-linear methods to model the underlying dynamics of a chaotic system such as the heart rate signal (Goldberger and West 1987; Pincus et al. 1991). Using the three domains of measurements of HRV (time, frequency and non-linear domains), we thus comprehensively investigate the heart rate dynamics in response to parachute jumping to highlight the cardiovascular risk potentially induced by environmental stress exposure in experienced skydivers performing free falls in a typical day of jumping.

It is of usual practice that experienced skydivers such as skydiving instructors perform repeated jumps in a day. This is, therefore, associated with repeated physical and cardiac workloads, as well as exposures to stress and hypoxia, which could induce physiological fatigue over the course of the day. Several studies have shown that cortical electroencephalographic (EEG) changes are significantly related to fatigue (Lal and Craig 2002; Nielsen et al. 2001). In addition, Truszczynski et al. (2009) showed that pilots under hypoxic conditions have their perceptual ability gradually decreased. It is of every parachutist's interest that experienced skydivers, and especially skydiving instructors for safety reasons, do not show any decrease in perceptual ability during a day of multiple jumps. We thus also investigated how jumps could hamper cortical arousal using Critical Flicker Fusion Frequency (CFFF). The CFFF is non invasive and reliable in measuring cortical arousal (Hou et al. 2007; Rota-Bartelink 1999) and has been demonstrated a good marker of cortical changes due to physical workload (Luczak and Sobolewski 2005; Luczak et al. 1995; Davranche and Pichon 2005), drug administration (Hunter et al. 1994; Hindmarch 1982), alcohol intoxication (Leigh 1982; Liu and Ho 2010; Schillaci and Fazio 1967), anaesthesia (Salib et al. 1992; Sharma et al. 2011; Wernberg et al. 1980), encephalopathy (Ali et al. 1994; Chang et al. 2007; Kircheis et al. 2002; Lauridsen et al. 2011) as well as hyperoxia (Balestra et al. 2012; Hemelryck et al. 2013). CFFF variations happen in parallel to EEG changes and are thus better than merely relying on subjective reports for neuropsychological defects (Seki and Hugon 1976). Using the CFFF, we can, therefore, perform an objective measurement of the effects of jumps on skydivers' arousal.

In this study we analyse linear, non-linear including fractal HRV, as well as CFFF to investigate the ANS and cerebral changes in experienced skydivers in a typical day of jumping. The aims are twofold: to explore the heart rate dynamics with investigation of the potential cardiovascular risk associated with parachute jumping and to assess the impact of stress, hypoxia exposure and fatigue due to the jump on "cerebral arousal" of experienced skydivers which may impact decision making processes.

Materials and methods

Study population

After ethical committee approval (B200-2013-043) and written informed consent, 18 experienced male skydivers (at least 300 jumps of experience: median = 1300; P25 = 487; P75 = 1625), aged 32 ± 5 years, volunteered for the study. Prior to entering the study, they were assessed fit to jump by a qualified doctor (medical examination as required by the medical commission of the French Skydiving Federation): none of the subjects had a history of previous cardiac abnormalities and none of them were on any cardio-active medication.

Timeline of measurements

Each skydiver performed successive jumps from a plane at 4000 m of height during a typical day of jumping. The position to adopt during free fall was not imposed for ethical reasons; however, in practice all parachute jumpers remained roughly horizontal. Time between the different jumps, time of jumps and number of jumps in the day were not imposed since parachute jump, as an acute highly stressful event, has no anticipatory effect on autonomic modulation of the heart (Hynynen et al. 2009). The ANS shows no acclimatization to repeated jumps (Allison et al. 2012): a stress, such as parachute jumping, that induces strong adrenocortical responses does not necessarily affect subsequent cortisol responses to the same stress (Deinzer et al. 1997).

Recording with the heart rate monitor began immediately after the participants got called to go to the plane 10 ± 5 min before take-off for each jump. Skydivers then underwent the CFFF test on their way to the

plane (=pre-jump). After take-off, the plane needs about 20 min to reach 4000 m of height. All skydivers sat at rest in the plane during the time of flight. At 3000 m (mean 3090 \pm 110 m) the skydivers did the CFFF test again (=jump). When the plane reached the drop point at 4000 m, the skydivers were asked to press the "lap time" button on the heart rate monitor at the exact time of door opening on the heart rate recording. Thus, the onset of the analysis of the session "jump" started exactly when door opening occurred for every jump. Only a few seconds are needed by skydivers to get ready after door opening before jumping and the time of free fall was about a minute before opening their parachutes at 1000 m. Five to 7 min are then required with the parachute before landing on ground. In this way all samples of 5 min of recording include few seconds at the door, the entire free fall and three to 4 min under the parachute. Immediately after landing, participants performed the CFFF test once more (=post-jump) before packing their parachutes. The heart rate monitor was then switched off after a minimum of 50 min of recording in total needed to measure heart rate and R-R intervals at three different moments. In the HRV Low-Frequency domain, 0.04 Hz corresponds to a cycle of 20 s. The minimum time necessary to interpret the frequency domain has to cover minimum 10 times the length of a cycle, which represents 200 s. About 3-4 min of recording in total is, therefore, the minimum time of measurement to be interpretable in that domain. Three samples of 5 min were then selected within each segment of the jump as follows: first, 15 min before the door opening = pre-jump; second, at the door opening = jump; and third, 15 min after the door opening = post-jump (Fig. 1).

Measurements

CFFF analysis

The day before measurements the skydiver subjects practiced using the CFFF device at least three times to get used to it; then measurements were taken the next day at the time points described above in the Timeline of Measurement section. The device consists of a rotating ring, surrounding a short cylindrical housing of 8 cm diameter containing the numeric (digital) frequency indicator. Attached to this housing is a flexible cable, on the end of which a single blue light-emitting diode (LED) (colour temperature 8000 K) is enclosed in a smaller cylindrical container (to shield it from stray light and reflections). While the subject to be tested is looking straight at the LED light at a distance individually adapted to his personal vision (generally around 50 cm), the investigator turns the dial slowly clockwise or anticlockwise to increase or decrease by steps of 0.25 Hz the

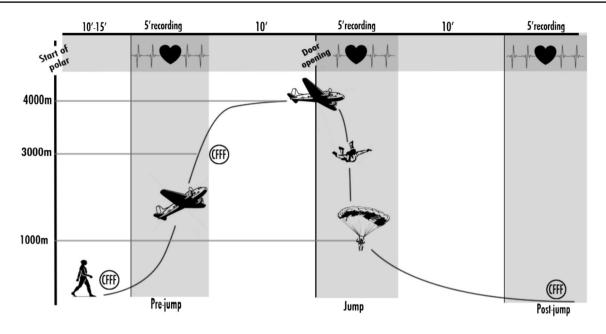


Fig. 1 Timeline of measurements. Recording of the heart rate began when skydivers were asked to go to the plane, 10 min before takeoff. Three samples of 5 min of the HRV recording were selected within each segment of the jump: first, 15 min before the door open-

flickering frequency of the LED. As there are no markings on the dial, nor a visible "starting position", the test subject has no indication of the actual flicker frequency. When the subject saw a change from flicker to fusion (or fusion to flicker), the actual frequency was noted immediately by the same investigator throughout all measurements for consistency. This fusion-threshold frequency is the definition of CFFF (Rota-Bartelink 1999; Tytla et al. 1990). The mean number of jumps during the day of measurements for each parachutist was 4 (\pm 1). The CFFF analysis was conducted on the three time points of measurements (pre-jump, jump and post-jump) for the first jump (="CFFF first jump") and the last jump (="CFFF last jump") of the day to highlight the effect of a single jump, as well as that of multiple jumps on cortical arousal.

Autonomic measures by HRV analysis

In this study, the S810i (Polar Electro Oy, Kempele, Finland) and RS800sd (Polar Electro, Oulu, Finland) heart rate monitors were used as a continuous monitoring of beat by beat HR. Reliability and validity to measure heart rate and heart rate variability of both S810i and RS800sd have been documented (Vanderlei et al. 2008; Radespiel-Troger et al. 2003). These devices are portable, compact and work wirelessly. Thus, they can be worn by skydivers performing jumps at 4000 m from a plane with no incidence on their safety and on the practice of free fall. The

ing = pre-jump; second, at the door opening = jump; third, 15 min after the door opening = post-jump. CFFF was measured 3 times: 5 min before take-off, at 3000 m during flight and immediately after landing

transmitter was secured around the chest of the skydivers by an elastic strap, and the wrist receiver was worn in the same way as a normal wristwatch. The wrist receiver provided two functions: real-time heart rate measurement (R–R intervals) and elapsed time of measurement. In keeping with the aim of the study to investigate the impact of parachute jumping on the cardiovascular system, as well as any risk associated with the practice of skydiving in general, the average for all jumps over a day is analysed for each subject. The Kubios software HRV 2.1 (UKU, Kuopio, Finland) was used to extract and analyse R–R intervals from the heart rate monitor's recordings (Fig. 2). This software is a complete solution for HRV analysis (Tarvainen et al. 2014) and provides three domains of measurements:

Time domain

Square root of the mean squared differences between successive RR intervals (RMSSD) and mean of HR and percentage of the differences of successive NN intervals greater than 50 ms normalised to all differences within the interval (pNN50) were analysed. RMSSD and pNN50 are recognised indexes of parasympathetic activity (Task force 1996; Kleiger et al. 1991; Manfrini et al. 2003) and pNN50 might be useful in clinical practice as it shows a strong relation with the later occurrence of coronary events (Manfrini et al. 2003).

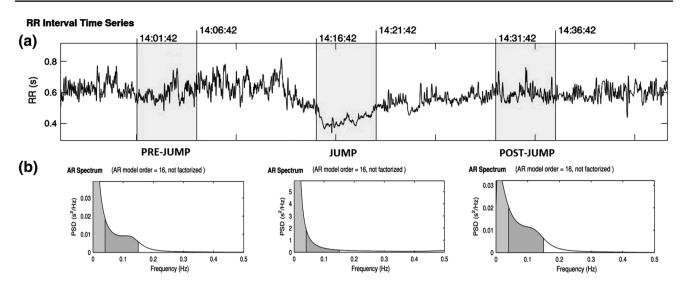


Fig. 2 (a) Original recording of RR intervals from one representative volunteer: *solid vertical lines* limit three grey areas that represent each period (*pre-jump*, *jump* and *post-jump*) of the HRV analysis. (b) Spectral analysis of RR intervals of *pre-jump*, *jump* and *post-*

jump periods from the same data. The different *grey areas* represent frequency power at very low frequency (0.00-0.04 Hz), at low frequency (0.04-0.10 Hz) and at high frequency (0.10-0.40 Hz) selected by an autoregressive model

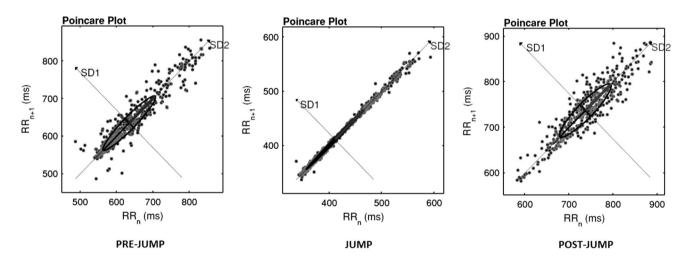


Fig. 3 Original Poincaré plots of pre-jump, jump and post-jump periods from one representative volunteer

Frequency domain

Frequency domain analysis yields information about the amount of overall variance in heart rate resulting from periodic oscillations of the heart rate at various frequencies (Stein et al. 1994). Two spectral components of the recording were analysed: high-frequency power (HF) and low-frequency power (LF). Power spectra were calculated by fitting a multivariate autoregressive (AR spectrum) model of order 16 to RR time series (Acharya et al. 2006). High-frequency power which is in the 0.15–0.4 Hz band is connected to the vagal activity and seems to provide a quantitative index of the influence of respiration on heart

rate signal (Berger et al. 1986). The power LF component which is in the 0.04–0.15 Hz band has been linked to the vagal and sympathetic activities (LF component increases with every form of sympathetic stimulation) (Acharya et al. 2004). Thus, LF/HF ratio is an important marker of sympathetic modulation or sympathovagal balance on heart rate variability control (Task Force 1996).

Non-linear domain

Analysis of heart rate dynamics by methods based on chaos theory and non-linear system theory has gained recent interest, in particular the Poincaré plot of the HRV signal (Fig. 3) which is used both for short-term (SD1) or longterm (SD2) analysis (Karmakar et al. 2011; Tulppo et al. 1996). It is constructed by plotting consecutive points of RR interval time series and is commonly used to assess the dynamics of the HRV signal (Tulppo et al. 1996; Hayano et al. 1999). The Poincaré plot is, therefore, a tool which can be applied to the analysis of R–R interval data gathered over a relatively short time period (Kamen et al. 1996) and describes the sympathetic and parasympathetic modulation of the heart rate (Kamen et al. 1996; Brennan et al. 2002). SD1 reflects the instantaneous beat-to-beat variability mediated by the vagal activity, and SD2 shows the global HR variability (Tulppo et al. 1996).

In addition, the fractal dimension (FrD) was calculated using the ORTO science software 4.9.85 (Alive System Llc, Kemerovo, Russia). The fractal dimension has been used in the analysis of electrocardiogram (ECG) and EEG to identify and distinguish specific states of physiologic function (Yeragani et al. 1998). To investigate the dynamics of the signal, sample entropy (SampEn) was also calculated which is a measure of the complexity or irregularity of the signal and considered less biased than the popular approximate entropy (Lake et al. 2002; Pincus 1995; Pincus and Goldberger 1994). The improved accuracy of SampEn statistics makes them useful in the study of experimental clinical cardiovascular and other biological time series (Richman and Moorman 2000). It has been established that complexity of beat-to-beat variability was controlled by the ANS (Porta et al. 2007a): heartbeat complexity could be reduced by vagal blockade (Penttila et al. 2003) when vagal activation increased complexity (Porta et al. 2007b). Sympathetic excitation by pharmacological (Penttila et al. 2003) or physiological method (Porta et al. 2007a) reduced complexity and sympathetic blockade with propranolol increased irregularity of the HR (Lepoluoto et al. 2005). FrD and SampEn of HR time series correlate highly with each other and also with the high-frequency power and hence appear to reflect vagal modulation of HR variability (Yeragani et al. 1993).

Statistical analysis

Statistical analyses were conducted using the GraphPad Prism 5 software (La Jolla, CA, USA). After normality assessment by Kolmogorov–Smirnov test, differences between pre-jump, jump and post-jump values for all parameters measured were assessed by ANOVA repeated measures test with Bonferroni's correction, or Friedmann test with Dunn's correction for non-parametric data.

All data are presented as mean \pm standard deviation. Statistical significance levels were set at p < 0.05 (*), p < 0.01 (**) and p < 0.001 (***), and "ns" denotes "no statistical significance".

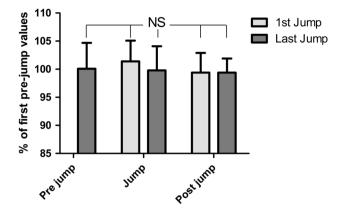


Fig. 4 Critical Flicker Fusion Frequency results, normalised to the pre-jump frequency of the first parachute jump of the day. No significant difference was found between any of the measurement time-points (before, during and after each jump) or between the first and last jump of the day for each parachutist

Results

CFFF results

No significant difference was found between the three time points in the CFFF measurements in either of the jumps. In addition, no significant difference was found between the CFFF measured at each time point, respectively, compared between the first and last jump of the day for each subject (Fig. 4).

HRV results

The HRV results are presented for the following time points: 15 min before (pre-jump), during (jump) and 15 min after (post-jump) a jump from 4000 m. height. Levels of significance and absolute values are presented in Table 1 for the Time domain, Table 2 for the Frequency domain and Table 3 for the non-linear domain. Figure 2 shows example results from one representative subject of (a) the RR interval changes and (b) the frequency domain HRV analysis of pre-jump, jump and post-jump. Figure 3 shows a Poincaré plot example from one representative volunteer for pre-jump, jump and post-jump.

Time domain analysis

Mean HR increased during the jump (p < 0.001) and came back to pre-jump values after the jump (p < 0.001) as shown in Table 1. pNN50 decreased during the jump (p < 0.001) and showed a tendency to increase after the jump, although this did not reach a level of significance (p > 0.05) thus pNN50 kept lower values after the jump in comparison with pre-jump (p < 0.05) (Table 1). RMSSD revealed lower values in both jump (p < 0.001) and post-jump (p < 0.001)

Table 1 Results of the time domain of the HRV analysis

Time domain						
	Pre-jump	Jump	Post-jump	Pre-jump vs jump	Jump vs post-jump	Pre-jump vs post-jump
λ Mean HR (bpm)	93.6 ± 11.4	121.9 ± 19.5	97.0 ± 15.3	***	***	NS
¥ pNN50 (%)	6.8 ± 4.2	4.0 ± 2.7	5.2 ± 4.0	***	ns	*
λ RMSSD (ms)	26.0 ± 7.7	19.1 ± 7.2	22.3 ± 7.3	***	**	***

Time domain includes mean heart rate (mean HR), successive NN intervals greater than 50 ms normalised to all differences within the interval (pNN50) and square root of the mean squared differences between successive RR intervals (rMSSD)

Results were analysed using the non parametric Friedman test and Dunn's post test when the results did not follow a Gaussian distribution (¥) and by the parametric ANOVA test and Bonferroni post test when the results followed a Gaussian distribution (λ) (NS *p* > 0.05; **p* < 0.05; **p* < 0.01; ****p* < 0.001)

Table 2	Results of the	frequency	domain	of the HRV	analysis
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Frequency domain							
	Pre-jump	Jump	Post-jump	Pre-jump vs jump	Jump vs post-jump	Pre-jump vs post-jump	
¥ HF power (ms ²)	214.1 ± 145.9	172.2 ± 110.6	137.0 ± 81.7	NS	*	**	
¥ HF (nu)	11.8 ± 6.3	14.5 ± 7.3	10.8 ± 9.1	NS	***	*	
¥ LF power (ms ²)	1612.0 ± 711.7	1278.0 ± 987.1	1397.0 ± 837.6	*	NS	NS	
¥ LF (nu)	88.0 ± 6.4	86.0 ± 6.0	89.6 ± 8.6	NS	***	**	
¥ LF/HF	8.9 ± 4.5	7.7 ± 4.3	11.8 ± 6.4	NS	***	**	

Frequency domain includes high-frequency power (HF power), low-frequency power (LF power), high frequency in normalised units (HF nu), low frequency in normalised units (LF nu) and low-frequency power/high-frequency power ratio (LF/HF)

Results were analysed using the non parametric Friedman test and Dunn's post test when the results did not follow a Gaussian distribution (¥) and by the parametric ANOVA test and Bonferroni post test when the results followed a Gaussian distribution (λ) (NS *p* > 0.05; **p* < 0.05; **p* < 0.01; ****p* < 0.001)

Non linear domain							
	Pre-jump	Jump	Post-jump	Pre-jump vs jump	Jump vs post-jump	Pre-jump vs post-jump	
λ SD1 (ms)	18.1 ± 5.6	13.2 ± 5.4	15.5 ± 5.3	***	***	***	
¥ SD2 (ms)	113.5 ± 36.3	106.7 ± 38.0	89.4 ± 25.9	NS	**	***	
¥ SampEn	0.8 ± 0.3	0.4 ± 0.2	0.8 ± 0.2	***	***	NS	
¥ FrD	1.2 ± 0.1	1.1 ± 0.1	1.2 ± 0.1	*	***	NS	

Table 3 Results of the non linear domain of the HRV analysis

Non linear domain includes the standard deviation of the points perpendicular to the line-of-identity of the Poincaré plot (SD1), the standard deviation along the line-of-identity of the Poincaré plot (SD2), sample entropy (SampEn) and fractal dimension (FrD)

Results were analysed using the non parametric Friedman test and Dunn's post test when the results did not follow a Gaussian distribution (¥) and by the parametric ANOVA test and Bonferroni post test when the results followed a Gaussian distribution (λ) (NS *p* > 0.05; **p* < 0.05; **p* < 0.01; ****p* < 0.001)

periods compared to pre-jump but showed an increase postjump in comparison with jump (p < 0.01) (Table 1).

Frequency domain analysis

No significant difference was found in the HF spectral density between pre-jump and jump (p > 0.05), but HF decreased significantly after the jump in comparison

with pre-jump (p < 0.01) and jump (p < 0.05), for more details see Table 2. LF spectral density decreased during the jump (p < 0.05) and the differences found post-jump in comparison with both pre-jump and jump were not significant (p > 0.05) (Table 2). Normalised indexes did not show significant differences between pre-jump and jump (p > 0.05). HFnu decreased after the jump compared to jump (p < 0.001) and pre-jump (p < 0.01) and LFnu

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revealed an increase after the jump in comparison with jump (p < 0.001) and pre-jump (p < 0.01) (Table 2). The LF/HF ratio increased significantly after the jump compared to pre-jump (p < 0.01) and jump (p < 0.001) but no significant difference was found between pre-jump and jump (p > 0.05) (Table 2).

Non-linear domain analysis

The modifications of SD2 demonstrated by the Poincaré plot analysis (Fig. 3) were not significant during the jump in comparison with pre-jump (Table 3). SD2 decreased post-jump compared to pre-jump (p < 0.001) and jump (p < 0.01) (Table 3). SD1 decreased during the jump (p < 0.001) and increased after the jump (p < 0.001), but the values post-jump remained lower compared to prejump (p < 0.001), see Table 3. SampEn decreased during the jump in comparison with pre-jump (p < 0.001) and increased after the jump (p < 0.001). FrD decreased during the jump compared to pre-jump (p < 0.05) and also increased post-jump compared to jump. Interestingly, both SampEn and FrD returned to pre-jump values after the jump (no significant differences were found between postjump and pre-jump values (p > 0.05) for both measurements): please refer to Table 3 for absolute values."

Discussion

The purpose of this study was (1) to further explore the heart rate dynamics and assess a potential cardiovascular risk in response to 4000 m jumps in experienced skydivers; (2) to assess whether there is an impact or not of such jumps on skydivers' cortical arousal, which may impact their decision making processes. In the present study, alterations in the cardiac autonomic control were measured by the use of the well-established non-invasive measures of HRV. In a normal heart, there will be continuous physiological variations of the sinus cycles reflecting a balanced sympathico-vagal state and normal HRV (van Ravenswaaij-Arts et al. 1993). In response to acute stress, such as skydiving, two principal physiological systems are primarily activated with different time dynamics. The ANS with adrenaline (epinephrine) released from the sympathetic branch is associated with short-term physiological changes such as heart rate. The hypothalamic-pituitary-adrenal (hpa) axis with the release of cortisol hormone enables further physiological resources to deal with the stressful stimulus. The data concerning ANS responses to skydiving by HRV analysis are only available from one study (Allison et al. 2012). In the latter nevertheless, Allison et al. focused on novelty and sensation seeking as essential influences on baseline functioning and propensities toward initial participation in high-risk activities, rather than explaining ANS activity during the jump in experienced skydivers. It has been shown that autonomic responses to external stimuli, including stress or attention, produce a decrease in parasympathetic tone and that there is a complementary increase in sympathetic tone only if the stimulus is of high intensity and prolonged duration (Porges 1995; Borresen and Lambert 2008; Yamamoto et al. 1991).

In this study, the time domain analysis shows a decrease of the parasympathetic tone of the skydiver at the time of the jump since both pNN50 and RMSSD decreased significantly. A few studies have shown that a parasympathetic decrease may be associated with high cardiovascular risk since an extremely low value of parasympathetic activity (pNN50 < 3 %) has predicted mortality by cardiac events (Manfrini et al. 2003). According to our results, the experienced skydiver might not be exposed to such a risk despite the value of pNN50 beeing very low during the jump (pNN50 = 4 %). Interestingly, the pNN50 did not increase significantly after the jump when RMSSD did compared to jump, and both measurements show a significant difference between pre-jump and post-jump with lower values post-jump compared to the ones pre-jump. This difference is not shown on the heart rate measurement. These more accurate measurements of the time domain of HRV lead us to consider the hormonal response to be responsible for these. The cortisol response is indeed significant at the time of jump but clearly peaks after the jump as pointed out by many authors (Taverniers et al. 2011; Hare et al. 2013; Deinzer et al. 1997).

The changes shown by the frequency domain are representative of three different situations:

- During the flight, hypoxia increases which should increase HR markedly (Liu et al. 2001) and decrease the HF component (Liu et al. 2001; Buchheit et al. 2004). Previous studies that were revealed in different protocols also showed that autonomic nervous activities were attenuated in hypoxic conditions and that the sympathetic activities were predominant compared with the parasympathetic at high altitude (Kanai et al. 2001; Vigo et al. 2010; Roche et al. 2002; Saito et al. 2005). Nevertheless, the values of the CFFF did not show significant differences in the three measurement time points, which suggests that hypoxia is well tolerated by the experienced skydiver and does not affect the ANS.
- Then, during the jump, it is expected that hypoxia will rapidly decrease, and a slight stress should be present. The rise in the HR clearly shows an increased sympathetic activity. Nevertheless, the LF power decreased significantly and the difference in measurements of LF/ HF ratio is not significant compared to the pre-jump

value. This unchanged ratio suggests that the sympathetic-parasympathetic balance was not affected by the jump and that there may be a co-activation of the vagal outflow with the sympathetic system. It is also noticeable that the HF range during the jump did not decrease, whereas RMSSD and pNN50 did. These apparent discrepancies may be explained by means of the altered respiratory frequency during the jump, increasing the respiratory sinusal arythmia (RSA). Jumping from a plane at 4000 m of height may cause changes in the respiration rate and depth (Fenz and Epstein 1967; Roth et al. 1996). These in turn can affect HRV (Penttila et al. 2001; Brown et al. 1993; Kitney et al. 1985), and subsequently increase the parasympathetic contribution (HF) by a shift from LF to HF, potentially masking the LF increase that should coincide with the rise of the sympathetic tone during the jump. Thus, correct interpretation of HRV measures by frequency domain has to account for possible changes in the respiration rate during the time course of data collection.

3. After the jump, the environmental conditions finally return to normoxia, with no particular effort or stress and a normal, free respiratory rate. Since the respiration should come back to a similar rate than pre-jump, the differences found between pre-jump and post-jump measures in the frequency domain with the increasing of LF/HF ratio and the decreasing of HF may be explained by the hormonal effect present after the jump.

In this study the tools utilised in the analysis require stationarity and when non-stationarities are present in the time and frequency-series analysed, this may distort the results. As such, it is important to discuss the findings against this stationarity issue. Although visual inspection and simple coefficient of variation were used to select the series (prejump = 12.2 %, jump = 15.9 % and post-jump = 15.8 %), this is not enough to guarantee a steady mean and steady variance as in (Porta et al. 2004). It was recently shown that the effect of including such non-stationarities is a bias towards finding a sympathetic dominance in sympathovagal balance (Magagnin et al. 2011). We can, therefore, not exclude that this is also the case in this study. Nevertheless, the protocol in this study was chosen specifically to minimise any such inclusion of non-stationarities, by replicating exactly that of the study for which authors showed a robust correlation (r = 0.7-0.8) of their skydiving HRV results between real and laboratory settings (Dikecligil and Mujica-Parodi 2010).

The analyses of non-linear domain show a highly significant decrease of SD1 which reflects the instantaneous beat-to-beat variability mediated by the vagal activity. This vagal input reduction is not clearly shown in the frequency

domain. This can be explained by the fact that the non-linear domain is much less affected by the RSA (Lewis and Short 2007; Penttila et al. 2001). Previous studies have indeed shown that the SD1 component is not influenced by any modified breathing patterns (Penttila et al. 2001). This supports the idea of the influence of the RSA on the frequency domain results at the time of the jump since the HF component did not decrease at this moment. Surprisingly, a difference is found in SD1 between pre-jump and post-jump values (post-jump significantly lower than prejump) and the SD2 component which represents the global and long-term HR variability is not affected by the jump but is clearly diminished after. Since the heart rate returned to pre-jump values and concurrently both RMSSD and pNN50 diminished after the jump, this suggests that the cardiovascular system remains affected after the jump. This observation goes in the direction of the neurohumoral response mainly present after the jump for the body to deal appropriately with the stressful stimulus.

Previously, some studies have shown that healthy heartbeat dynamics have a fractal-like temporal structure, with self-similar fluctuations over a wide range of time scales (Goldberger 1996). Nunes Amaral et al. (1998) noted that scale-independent measures such as the fractal dimension can distinguish healthy from pathologic cardiac behaviour. Even if there is no strong consensus, it seems that a value of FrD superior to 1.5 is the sign of a perturbed balance between the sympathetic and parasympathetic branch of the ANS (Struzik et al. 2004) putting the skydiver at risk of syncope, especially if the value of FrD is greater than 1.8 and the HF index is low (Butler et al. 1993). The decrease of FrD during the jump to a value of 1.1 suggests a low random behaviour of the heart rhythm which may keep the skydiver away of such a pathological threshold during the jump. In our study, SampEn quantifies the regularity of the R-R interval. The more regular and predictable the R-R interval series, the lower the value of SampEn. On the other hand the more randomness in the R-R interval series, the higher its value. The evolution of SampEn follows the same variations as FrD with a significant decreasing between pre-jump and jump values. This shows a low level of complexity of the heart rythm and supports the fact that there is a sympathetic activation during the jump since altered fractal properties of HR dynamics are closely related to elevated noradrenaline levels (Tulppo et al. 2001).

After the jump, interestingly a return of SampEn and FrD to pre-jump values is observed, which suggests that the cardiac workload induced by skydiving is easily compensated through a return to an adjustable state of the cardiovascular system after the jump despite the hormonal effect being present. This points towards a good healthy state of the experienced skydivers excluding at least partially the possibility for adverse long-term effects. In this study only experienced skydivers were measured; however, it would be of great interest to conduct further studies investigating such a healthy state in beginners.

During the flight, the barometric pressure falls with increasing altitude consequently inducing a reduction in the partial pressure of oxygen. This results in a hypoxic challenge for any individual ascending to altitude. In this study we also aimed to investigate how the hypoxic conditions due to exposures to the height of 4000 m could affect the skydivers' alertness. Recent studies have indeed stressed the impact of acute hypoxia on cerebral oxygenation (Ainslie et al. 2007) and cerebral arousal (Truszczynski et al. 2009). Indices to quantify the effects of parachute jumping on perceptual ability can be roughly divided into two approaches. The first is a behavioural approach, measuring task performance such as mental arithmetic, memory, visuo-spatial learning, reaction time or manual dexterity. Although these behavioural studies have been largely used, many of these tests have been criticised because of the influences of motivation, experience and learning on the test results. Also in the context of our study, such measures are too long to be feasible in a plane just before jumping. The second approach relies on observing a change in objective, measurable neurological parameters. The CFFF has been demonstrated to provide such a reliable and validated measurement technique (Chang et al. 2007; Hindmarch 1988; Hemelryck et al. 2013). In their study, Truszczynski et al. showed that the higher the decrease in oxygen saturation under hypoxic conditions, the higher the decrease in CFFF, suggesting that hypoxia may gradually decrease perceptual ability. The practice of skydiving, as any sport, may by itself induce physiological fatigue. Several studies have furthermore suggested that there is a correlation between cortical electroencephalographic impairment and fatigue (Lal and Craig 2002; Nielsen et al. 2001). All these environmental stresses had led us to think that repeated jumps at 4000 m of height may affect the skydivers' perceptual vigilance. However, our study suggests that there is no cerebral impairment due to skydiving since there is no significant difference found between the three measurement time points in "CFFF first jump" values. In addition, the fact that the CFFF measured at each before, during and after jumping does not significantly differ between the first and last session of the day suggests that experienced skydivers do not show any decrease in perceptual ability during a day of multiple jumps. These are important considerations in situations, like skydiving, where precise and accurate judgment and actions are essentially life-critical.

Conclusion

The present study shows a vagal input reduction with a rise of the sympathetic activity during the jump and that

the cardiac workload induced by parachute jumping is well tolerated and does not increase the cardiovascular risk for the experienced skydiver. These findings could be achieved through the investigation of the heart rate dynamics by means of non-linear analysis. This study also shows that neither hypoxia, nor fatigue or stress could hamper the coordination or decision-making process of the experienced skydiver.

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Conflict of interest None.

References

- Acharya U, Kannathal N, Sing O, Ping L, Chua T (2004) Heart rate analysis in normal subject of various age groups. Biomed Eng Online 3(1):24
- Acharya UR, Paul Joseph K, Kannathal N, Lim CM, Suri JS (2006) Heart rate variability: a review. Med Biol Eng Comput 44(12):1031–1051
- Ainslie PN, Barach A, Murrell C, Hamlin M, Hellemans J, Ogoh S (2007) Alterations in cerebral autoregulation and cerebral blood flow velocity during acute hypoxia: rest and exercise. Am J Physiol Heart Circ Physiol 292(2):H976–H983. doi:10.1152/ ajpheart.00639.2006
- Ali MR, Khaleque A, Khanam M, al-Shatti A, Ahmed RU (1994) Critical flicker frequency of mentally retarded and normal persons. Percept Mot Skills 79(3 Pt 1):1235–1238
- Allison AP, Peres JC, Boettger C, Leonbacher U, Shitcliff A, Elizabeth A (2012) Fight, flight, or fall: autonomic nervous system reactivity during skydiving. Personal Individ Diff 53:218–223
- Analitis A, Katsouyanni K, Biggeri A, Baccini M, Forsberg B, Bisanti L, Kirchmayer U, Ballester F, Cadum E, Goodman PG, Hojs A, Sunyer J, Tiittanen P, Michelozzi P (2008) Effects of cold weather on mortality: results from 15 European cities within the PHEWE project. Am J Epidemiol 168(12):1397–1408. doi:10.1093/aje/kwn266
- Balestra C, Lafere P, Germonpre P (2012) Persistence of critical flicker fusion frequency impairment after a 33 mfw SCUBA dive: evidence of prolonged nitrogen narcosis? Eur J Appl Physiol 112(12):4063–4068. doi:10.1007/s00421-012-2391-z
- Berger RD, Akselrod S, Gordon D, Cohen RJ (1986) An efficient algorithm for spectral analysis of heart rate variability. IEEE Trans Biomed Eng 33(9):900–904. doi:10.1109/ TBME.1986.325789
- Borresen J, Lambert MI (2008) Autonomic control of heart rate during and after exercise: measurements and implications for monitoring training status. Sports Med 38(8):633–646
- Brennan M, Palaniswami M, Kamen P (2002) Poincare plot interpretation using a physiological model of HRV based on a network of oscillators. Am J Physiol Heart Circ Physiol 283(5):H1873– H1886. doi:10.1152/ajpheart.00405.2000
- Brown TE, Beightol LA, Koh J, Eckberg DL (1993) Important influence of respiration on human R-R interval power spectra is largely ignored. J Appl Physiol 75(5):2310–2317

- Buchheit M, Richard R, Doutreleau S, Lonsdorfer-Wolf E, Brandenberger G, Simon C (2004) Effect of acute hypoxia on heart rate variability at rest and during exercise. Int J Sports Med 25(4):264–269. doi:10.1055/s-2004-819938
- Butler GC, Yamamoto Y, Xing HC, Northey DR, Hughson RL (1993) Heart rate variability and fractal dimension during orthostatic challenges. J Appl Physiol 75(6):2602–2612
- Cavenett T, Nixon RD (2006) The effect of arousal on memory for emotionally-relevant information: a study of skydivers. Behav Res Ther 44(10):1461–1469. doi:10.1016/j.brat.2005.11.002
- Chang TT, Ciuffreda KJ, Kapoor N (2007) Critical flicker frequency and related symptoms in mild traumatic brain injury. Brain Injury 21(10):1055–1062. doi:10.1080/02699050701591437
- Chatterton RT Jr, Vogelsong KM, Lu YC, Hudgens GA (1997) Hormonal responses to psychological stress in men preparing for skydiving. J Clin Endocrinol Metab 82(8):2503–2509. doi:10.1210/jcem.82.8.4133
- Chen YC, Lin FC, Shiao GM, Chang SC (2008) Effect of rapid ascent to high altitude on autonomic cardiovascular modulation. Am J Med Sci 336(3):248–253. doi:10.1097/MAJ.0b013e3181629a32
- Cowan MJ (1995) Measurement of heart rate variability. West J Nurs Res 17(1):32–48 (discussion 101–111)
- Cripps TR, Malik M, Farrell TG, Camm AJ (1991) Prognostic value of reduced heart rate variability after myocardial infarction: clinical evaluation of a new analysis method. Br Heart J 65(1):14–19
- Davranche KP, Pichon A (2005) Critical flicker frequency threshold increment after an exhausting exercise. J Sport Exerc Psychol 27:515–520
- Deinzer R, Kirschbaum C, Gresele C, Hellhammer DH (1997) Adrenocortical responses to repeated parachute jumping and subsequent h-CRH challenge in inexperienced healthy subjects. Physiol Behav 61(4):507–511
- Dikecligil GN, Mujica-Parodi LR (2010) Ambulatory and challengeassociated heart rate variability measures predict cardiac responses to real-world acute emotional stress. Biol Psychiatry 67(12):1185–1190. doi:10.1016/j.biopsych.2010.02.001
- Fenz WD, Epstein S (1967) Gradients of physiological arousal in parachutists as a function of an approaching jump. Psychosom Med 29(1):33–51
- Goldberger AL (1996) Non-linear dynamics for clinicians: chaos theory, fractals, and complexity at the bedside. Lancet 347(9011):1312–1314
- Goldberger AL (2006) Giles f. Filley lecture. Complex systems. Proc Am Thoracic Soc 3(6):467–471. doi:10.1513/ pats.200603-028MS
- Goldberger AL, West BJ (1987) Fractals in physiology and medicine. Yale J Biol Med 60(5):421–435
- Gorman JM, Sloan RP (2000) Heart rate variability in depressive and anxiety disorders. Am Heart J 140(4 Suppl):77–83
- Goseki Y, Matsubara T, Takahashi N, Takeuchi T, Ibukiyama C (1994) Heart rate variability before the occurrence of silent myocardial ischemia during ambulatory monitoring. Am J Cardiol 73(12):845–849
- Granberg PO (1991) Human physiology under cold exposure. Arctic Med Res 50(suppl 6):23–27
- Grossman P (1983) Respiration, stress, and cardiovascular function. Psychophysiology 20(3):284–300
- Hare OA, Wetherell MA, Smith MA (2013) State anxiety and cortisol reactivity to skydiving in novice versus experienced skydivers. Physiol Behav 118:40–44. doi:10.1016/j.physbeh.2013.05.011
- Hayano J, Takahashi H, Toriyama T, Mukai S, Okada A, Sakata S, Yamada A, Ohte N, Kawahara H (1999) Prognostic value of heart rate variability during long-term follow-up in chronic haemodialysis patients with end-stage renal disease. Nephrol Dial Transplant 14(6):1480–1488

- Hemelryck W, Rozloznik M, Germonpre P, Balestra C, Lafere P (2013) Functional comparison between critical flicker fusion frequency and simple cognitive tests in subjects breathing air or oxygen in normobaria. Diving Hyperb Med J South Pacific Underw Med Soc 43(3):138–142
- Hindmarch I (1982) Critical flicker fusion frequency (CFF): the effects of psychotropic compounds. Pharmacopsychiatry 15:44–48
- Hindmarch I (1988) Information processing, critical flicker fusion threshold and benzodiazepines: results and speculations. Psychopharmacol Ser 6:79–89
- Hnatkova K, Copie X, Staunton A, Malik M (1995) Numeric processing of Lorenz plots of R-R intervals from long-term ECGs. Comparison with time-domain measures of heart rate variability for risk stratification after myocardial infarction. J Electrocardiol 28(Suppl):74–80
- Hou RH, Langley RW, Szabadi E, Bradshaw CM (2007) Comparison of diphenhydramine and modafinil on arousal and autonomic functions in healthy volunteers. J Psychopharmacol 21(6):567– 578. doi:10.1177/0269881106071022
- Hultgren HN (1992) Effects of altitude upon cardiovascular diseases. J Wilderness Med 3(3):301–308
- Hunter KM, Zacharias M, Parkinson R, Luyk NH (1994) Effect of flumazenil on the recovery from intravenous midazolam. N Z Dental J 90(399):9–12
- Hynynen E, Konttinen N, Rusko H (2009) Heart rate variability and stress hormones in novice and experienced parachutists anticipating a jump. Aviat Space Environ Med 80(11):976–980
- Kamen PW, Krum H, Tonkin AM (1996) Poincare plot of heart rate variability allows quantitative display of parasympathetic nervous activity in humans. Clin Sci 91(2):201–208
- Kanai M, Nishihara F, Shiga T, Shimada H, Saito S (2001) Alterations in autonomic nerve control of heart rate among tourists at 2700 and 3700 m above sea level. Wilderness Environ Med 12:8–12
- Karmakar CK, Khandoker AH, Voss A, Palaniswami M (2011) Sensitivity of temporal heart rate variability in Poincare plot to changes in parasympathetic nervous system activity. Biomed Eng Online 10:17. doi:10.1186/1475-925X-10-17
- Kircheis G, Wettstein M, Timmermann L, Schnitzler A, Haussinger D (2002) Critical flicker frequency for quantification of lowgrade hepatic encephalopathy. Hepatology 35(2):357–366. doi:10.1053/jhep.2002.30957
- Kitney RI, Fulton T, McDonald AH, Linkens DA (1985) Transient interactions between blood pressure, respiration and heart rate in man. J Biomed Eng 7(3):217–224
- Kleiger RE, Bigger JT, Bosner MS, Chung MK, Cook JR, Rolnitzky LM, Steinman R, Fleiss JL (1991) Stability over time of variables measuring heart rate variability in normal subjects. Am J Cardiol 68(6):626–630
- Kleiger RE, Stein PK, Bosner MS, Rottman JN (1992) Time domain measurements of heart rate variability. Cardiol Clin 10(3):487–498
- Krstacic G, Krstacic A, Smalcelj A, Milicic D, Jembrek-Gostovic M (2007) The "Chaos Theory" and nonlinear dynamics in heart rate variability analysis: does it work in short-time series in patients with coronary heart disease? Ann Noninvasive Electrocardiol 12(2):130–136. doi:10.1111/j.1542-474X.2007.00151.x
- Lake DE, Richman JS, Griffin MP, Moorman JR (2002) Sample entropy analysis of neonatal heart rate variability. Am J Physiol Regul Integr Comp Physiol 283(3):R789–R797. doi:10.1152/ ajpregu.00069.2002
- Lal SK, Craig A (2002) Driver fatigue: electroencephalography and psychological assessment. Psychophysiology 39(3):313–321 doi:10.1017.S0048577201393095
- Lauridsen MM, Jepsen P, Vilstrup H (2011) Critical flicker frequency and continuous reaction times for the diagnosis of

minimal hepatic encephalopathy: a comparative study of 154 patients with liver disease. Metab Brain Dis 26(2):135–139. doi:10.1007/s11011-011-9242-1

- Leach JG, Griffith R (2008) Restrictions in working memory capacity during parachuting: a possible cause of 'no pull' failures. Appl Cogn Psychol 57:147–157
- Leigh G (1982) The combined effects of alcohol consumption and cigarette smoking on critical flicker frequency. Addict Behav 7(3):251–259
- Lepoluoto A, Nino J, Tahvanainen K, Ylitalo R, Kuusela T, Kahonen M, Kaila T (2005) Propranolol increases the complexity of heart rate fluctuations–a mode of antiarrhythmic action? Int J Clin Pharmacol Ther 43(2):101–108
- Lewis MJ, Short AL (2007) Sample entropy of electrocardiographic RR and QT time-series data during rest and exercise. Physiol Meas 28(6):731–744. doi:10.1088/0967-3334/28/6/011
- Liu YC, Ho CH (2010) Effects of different blood alcohol concentrations and post-alcohol impairment on driving behavior and task performance. Traffic Injury Prev 11(4):334–341. doi:10.1080/15389581003747522
- Liu XX, Lu LL, Zhong CF, Cheng ZH, Yuan Q, Ren HR (2001) Analysis of heart rate variability during acute exposure to hypoxia. Space Med Med Eng 14(5):328–331
- Luczak A, Sobolewski A (2005) Longitudinal changes in critical flicker fusion frequency: an indicator of human workload. Ergonomics 48(15):1770–1792. doi:10.1080/00140130500241753
- Luczak A, Kurkus-Rozowska B, Sobolewski A (1995) Flicker test as a load measurement during the combined effect of heat and noise. Int J Occup Saf Ergon 1(2):160–166
- Magagnin V, Bassani T, Bari V, Turiel M, Maestri R, Pinna GD, Porta A (2011) Non-stationarities significantly distort short-term spectral, symbolic and entropy heart rate variability indices. Physiol Meas 32(11):1775–1786. doi:10.1088/0967-3334/32/11/S05
- Malliani A, Pagani M, Lombardi F, Cerutti S (1991) Cardiovascular neural regulation explored in the frequency domain. Circulation 84(2):482–492
- Malliani A, Lombardi F, Pagani M (1994) Power spectrum analysis of heart rate variability: a tool to explore neural regulatory mechanisms. Br Heart J 71(1):1–2
- Manfrini O, Pizzi C, Trere D, Fontana F, Bugiardini R (2003) Parasympathetic failure and risk of subsequent coronary events in unstable angina and non-ST-segment elevation myocardial infarction. Eur Heart J 24(17):1560–1566
- Mogford JE, Tawil N, Chen A, Gies D, Xia Y, Mustoe TA (2002) Effect of age and hypoxia on TGFbeta1 receptor expression and signal transduction in human dermal fibroblasts: impact on cell migration. J Cell Physiol 190(2):259–265. doi:10.1002/jcp.10060
- Mujica-Parodi LR, Renelique R, Taylor MK (2009a) Higher body fat percentage is associated with increased cortisol reactivity and impaired cognitive resilience in response to acute emotional stress. Int J Obesity 33(1):157–165. doi:10.1038/ijo.2008.218
- Mujica-Parodi LR, Strey HH, Frederick B, Savoy R, Cox D, Botanov Y, Tolkunov D, Rubin D, Weber J (2009b) Chemosensory cues to conspecific emotional stress activate amygdala in humans. PLoS One 4(7):e6415. doi:10.1371/journal.pone.0006415
- Mullen TJ, Appel ML, Mukkamala R, Mathias JM, Cohen RJ (1997) System identification of closed-loop cardiovascular control: effects of posture and autonomic blockade. Am J Physiol 272(1 Pt 2):H448–H461
- Niebauer J, Cooke JP (1996) Cardiovascular effects of exercise: role of endothelial shear stress. J Am Coll Cardiol 28(7):1652–1660. doi:10.1016/S0735-1097(96)00393-2
- Nielsen B, Hyldig T, Bidstrup F, Gonzalez-Alonso J, Christoffersen GR (2001) Brain activity and fatigue during prolonged exercise in the heat. Pflugers Arch 442(1):41–48

- Nunes Amaral LA, Goldberger AL, Ivanov P, Stanley HE (1998) Scale-independent measures and pathologic cardiac dynamics. Phys Rev Lett 81(11):2388–2391
- Penttila J, Helminen A, Jartti T, Kuusela T, Huikuri HV, Tulppo MP, Coffeng R, Scheinin H (2001) Time domain, geometrical and frequency domain analysis of cardiac vagal outflow: effects of various respiratory patterns. Clin Physiol 21(3):365–376
- Penttila J, Helminen A, Jartti T, Kuusela T, Huikuri HV, Tulppo MP, Scheinin H (2003) Effect of cardiac vagal outflow on complexity and fractal correlation properties of heart rate dynamics. Auton Autacoid Pharmacol 23(3):173–179
- Pincus S (1995) Approximate entropy (ApEn) as a complexity measure. Chaos 5(1):110–117. doi:10.1063/1.166092
- Pincus SM, Goldberger AL (1994) Physiological time-series analysis: what does regularity quantify? Am J Physiol 266(4 Pt 2):H1643–H1656
- Pincus SM, Gladstone IM, Ehrenkranz RA (1991) A regularity statistic for medical data analysis. J Clin Monit 7(4):335–345
- Porges SW (1995) Cardiac vagal tone: a physiological index of stress. Neurosci Biobehav Rev 19(2):225–233
- Porta A, D'Addio G, Guzzetti S, Lucini D, Pagani M (2004) Testing the presence of non stationarities in short heart rate variability series. Comput Cardiol 31:645–648
- Porta A, Gnecchi-Ruscone T, Tobaldini E, Guzzetti S, Furlan R, Montano N (2007a) Progressive decrease of heart period variability entropy-based complexity during graded headup tilt. J Appl Physiol 103(4):1143–1149. doi:10.1152/ japplphysiol.00293.2007
- Porta A, Guzzetti S, Furlan R, Gnecchi-Ruscone T, Montano N, Malliani A (2007b) Complexity and nonlinearity in short-term heart period variability: comparison of methods based on local nonlinear prediction. IEEE Trans Biomed Eng 54(1):94–106. doi:10.1109/TBME.2006.883789
- Radespiel-Troger M, Rauh R, Mahlke C, Gottschalk T, Muck-Weymann M (2003) Agreement of two different methods for measurement of heart rate variability. Clin Auton Res 13(2):99–102. doi:10.1007/s10286-003-0085-7
- Reid DH, Doerr JE, Doshier HD, Ellertson DG (1971) Heart rate and respiration rate response to parachuting: physiological studies of military parachutists via FM-FM telemetry. II. Aerosp Med 42(11):1200–1207
- Richman JS, Moorman JR (2000) Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol Heart Circ Physiol 278(6):H2039–H2049
- Roche F, Reynaud C, Garet M, Pichot V, Costes F, Barthelemy JC (2002) Cardiac baroreflex control in humans during and immediately after brief exposure to simulated high altitude. Clin Physiol Funct Imaging 22:301–306
- Rota-Bartelink A (1999) The diagnostic value of automated flicker threshold perimetry. Curr Opin Ophthalmol 10(2):135–139
- Roth WT, Breivik G, Jorgensen PE, Hofmann S (1996) Activation in novice and expert parachutists while jumping. Psychophysiology 33(1):63–72
- Saito S, Tanobe K, Yamada M, Nishihara F (2005) Relationship between arterial oxygen saturation and heart rate variability at high altitude. Am J Emerg Med 23:8–12
- Salib Y, Plourde G, Alloul K, Provost A, Moore A (1992) Measuring recovery from general anaesthesia using critical flicker frequency: a comparison of two methods. Can J anaesth 39(10):1045–1050. doi:10.1007/BF03008373
- Schedlowski M, Tewes U (1992) Physiological arousal and perception of bodily state during parachute jumping. Psychophysiology 29(1):95–103
- Schillaci C, Fazio O (1967) Critical fusion frequency. Its changes after ingestion of alcohol. Bollettino d'oculistica 46(10):772–782

- Seki K, Hugon M (1976) Critical flicker frequency (CFF) and subjective fatigue during an oxyhelium saturation dive at 62 ATA. Undersea Biomed Res 3(3):235–247
- Shane WP, Slinde KE (1968) Continuous ECG recording during freefall parachuting. Aerosp Med 39(6):597–603
- Sharma P, Singh S, Sharma BC, Kumar M, Garg H, Kumar A, Sarin SK (2011) Propofol sedation during endoscopy in patients with cirrhosis, and utility of psychometric tests and critical flicker frequency in assessment of recovery from sedation. Endoscopy 43(5):400–405 doi:10.1055
- Stein PK, Bosner MS, Kleiger RE, Conger BM (1994) Heart rate variability: a measure of cardiac autonomic tone. Am Heart J 127(5):1376–1381
- Struzik ZR, Hayano J, Sakata S, Kwak S, Yamamoto Y (2004) 1/f scaling in heart rate requires antagonistic autonomic control. Phys Rev E 70(5 Pt 1):050901
- Sztajzel J (2004) Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. Swiss Med Wkly 134(35–36):514–522 (2004/35/smw-10321)
- Tarvainen MP, Niskanen JP, Lipponen JA, Ranta-Aho PO, Karjalainen PA (2014) Kubios HRV–heart rate variability analysis software. Comput Methods Programs Biomed 113(1):210–220. doi:10.1016/j.cmpb.2013.07.024
- Task Force (1996) Heart rate variability: standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Circulation 93(5):1043–1065
- Taverniers J, Smeets T, Lo Bue S, Syroit J, Van Ruysseveldt J, Pattyn N, von Grumbkow J (2011) Visuo-spatial path learning, stress, and cortisol secretion following military cadets' first parachute jump: the effect of increasing task complexity. Cogn Affect Behav Neurosci 11(3):332–343. doi:10.3758/s13415-011-0043-0
- Truszczynski O, Wojtkowiak M, Biernacki M, Kowalczuk K (2009) The effect of hypoxia on the critical flicker fusion threshold in pilots. Int J Occup Med Environ Health 22(1):13–18. doi:10.2478/v10001-009-0002-y
- Tulppo MP, Makikallio TH, Takala TE, Seppanen T, Huikuri HV (1996) Quantitative beat-to-beat analysis of heart rate dynamics during exercise. Am J Physiol 271(1 Pt 2):H244–H252
- Tulppo MP, Makikallio TH, Seppanen T, Shoemaker K, Tutungi E, Hughson RL, Huikuri HV (2001) Effects of pharmacological

adrenergic and vagal modulation on fractal heart rate dynamics. Clin Physiol 21(5):515–523

- Tytla ME, Trope GE, Buncic JR (1990) Flicker sensitivity in treated ocular hypertension. Ophthalmology 97(1):36–43
- Valentini M, Parati G (2009) Variables influencing heart rate. Prog Cardiovasc Dis 52(1):11–19. doi:10.1016/j.pcad.2009.05.004
- van Ravenswaaij-Arts CM, Kollee LA, Hopman JC, Stoelinga GB, van Geijn HP (1993) Heart rate variability. Ann Int Med 118(6):436–447
- Vanderlei LC, Silva RA, Pastre CM, Azevedo FM, Godoy MF (2008) Comparison of the Polar S810i monitor and the ECG for the analysis of heart rate variability in the time and frequency domains. Braz J Med Biol Res 41(10):854–859
- Vigo DE, Lloret SP, Videla AJ, Chada D, Hunichen H, Mercuri J, Romero R, Siri L, Cardinali D (2010) Heart rate nonlinear dynamics during sudden hypoxia at 8230 m simulated altitude. Wilderness Environ Med 20:4–10
- Wagner JA, Robinson S, Marino RP (1974) Age and temperature regulation of humans in neutral and cold environments. J Appl Physiol 37(4):562–565
- Wernberg M, Nielsen SF, Hommelgaard P (1980) A comparison between reaction time measurement and critical flicker fusion frequency under rising nitrous oxide inhalation in healthy subjects. Acta Anaesthesiol Scand 24(2):86–89
- Yamamoto Y, Hughson RL, Peterson JC (1991) Autonomic control of heart rate during exercise studied by heart rate variability spectral analysis. J Appl Physiol 71(3):1136–1142
- Yeragani VK, Srinivasan K, Vempati S, Pohl R, Balon R (1993) Fractal dimension of heart rate time series: an effective measure of autonomic function. J Appl Physiol 75(6):2429–2438
- Yeragani VK, Sobolewski E, Jampala VC, Kay J, Yeragani S, Igel G (1998) Fractal dimension and approximate entropy of heart period and heart rate: awake versus sleep differences and methodological issues. Clin Sci 95(3):295–301
- Zhang D, She J, Zhang Z, Yu M (2014) Effects of acute hypoxia on heart rate variability, sample entropy and cardiorespiratory phase synchronization. Biomed Eng Online 13:73. doi:10.1186/1475-925X-13-73