CZECH TECHNICAL UNIVERSITY IN PRAGUE

FACULTY OF TRANSPORTATION SCIENCES

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COMPLEX ASSESSMENT OF PILOT FATIGUE IN TERMS OF PHYSIOLOGICAL PARAMETERS

Bachelor's Thesis

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Declaration

I hereby submit for assessment and defense a bachelor's thesis, prepared at the end of my studies at the Czech Technical University in Prague, the Faculty of Transportation Sciences.

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Abstrakt

Únava pilotů je jedním z hlavních důvodů leteckých nehod, ke kterým došlo v důsledku pochybení lidského činitele. Z tohoto důvodu je v zájmu zachování nejvyšších standardů letové bezpečnosti ve všech fázích letu zásadní být schopen zabránit vzniku únavy nebo alespoň být schopen ji účinně detekovat a následně na tuto skutečnost upozornit posádku, aby byla schopna unaveného člena posádky odstavit. V současnosti existují studie zabývající se detekcí a sledováním únavy pilotů prostřednictvím fyziologických parametrů, jako je srdeční aktivita, pohyby očí, aktivita horních končetin apod. Ze všech dostupných fyziologických měření se pak analýza variability srdečního rytmu (HRV) jeví jako nejvhodnější metoda zkoumání únavy pilota. Ačkoli se k hodnocení únavy používá mnoho parametrů vycházejících z analýzy variability srdečního rytmu, v literatuře neexistuje shoda o tom, které z těchto parametrů variability srdeční frekvence jsou nejdůležitější pro použití při detekci únavy piloty. Na základě tohoto nedostatku informací v kontextu současného stavu poznání je cílem této práce zjistit nejvýznamnější parametry analýzy variability srdečního rytmu, které lze přímo použít při monitorování únavy pilota. Pro účely zisku dat byly provedeny 24hodinové experimenty, při nichž byla sbírána data o srdeční aktivitě 16 subjektů na Ústavu letecké dopravy, Fakulty dopravní, Českého vysokého učení technického v Praze. Údaje o srdeční aktivitě subjektu byly zaznamenány ve formě elektrokardiogramu (EKG), zatímco plnily letové úkoly. První část této práce přináší teoretické základy únavy v prostředí kokpitu a vysvětluje několik metod, které se používají pro analýzu variability srdeční frekvence zaznamenaných signálů EKG. Následující části obsahují metody statistické analýzy používané k zjištění parametrů s nejvyšší importancí. Výsledky naznačují, že parametr pVLF analýzy ve frekvenční a časově-frekvenční doméně a parametr nHF analýzy HRV ve frekvenční doméně jsou parametry s nejvyšší importancí v případě indikace únavy člena letové posádky.

Klíčová slova: Únava pilota, fyziologické parametry, srdeční aktivita, variabilita srdečního rytmu.

Abstract

Pilot fatigue is one of the main reasons of aircraft accidents that were caused due to the human error factors in flight crew. Therefore, in order to maintain the highest standards of flight safety throughout all flight phases, it is crucially important to be able to prevent occurrence of fatigue or at least to be able to efficiently detect it, afterwards alert the crew to eliminate the fatigued member from flying. At present, there are many studies focusing on detection and monitoring of pilot fatigue by tracking pilot's physiological parameters such as: cardiac activity, eye movements, upper-limb activities etc. Among all those physiological measurements available, heart rate variability analysis seems to be the most accurate method to examine pilot fatigue. Although many indices of heart rate variability analysis are used to evaluate fatigue, there is no consensus in the literature on which of those heart rate variability indices are the most important ones to utilize on determination of pilot fatigue. Based on this lack of information on the current state of the art, the purpose of this thesis is to ascertain the most significant parameters of heart rate variability analysis that can be directly used in determining pilot fatigue. For obtaining data, a 24-hours of cardiac activity measurements were conducted on 16 subjects on a flight simulator located at the Department of Air Transport, Faculty of Transportation Sciences, Czech Technical University in Prague. The subject's cardiac activity data were recorded in form of electrocardiogram (ECG) while they performed flying tasks. The first part of this thesis delivers a theoretical background on fatigue in the cockpit environment and explains several methods that are used for heart rate variability analysis of the recorded ECG signals. The following parts provide the statistical analysis methods used to find out the most important parameters. The results indicate that pVLF index of the frequency domain and time-frequency domain analysis and nHF parameter of frequency-domain analysis of HRV corresponds to the most important indices which indicate fatigued condition of a flight crew member.

Keywords: Pilot fatigue, physiological parameters, cardiac activity, heart rate variability.

List of abbreviations

ADF	Automatic Direction Finder
AIP	Aeronautical Information Publication
ALT	Altitude
AME	Authorized Medical Examiner
ANS	Autonomic Nervous System
ATC	Air Traffic Control
ATIS	Automatic Terminal Information Service
ATO	Approved Training Organization
ATP	Adenosine Triphosphate
ATPL(A)	Airline Transport Pilot License (Aircraft)
CAT	Category (for landing)
CDI	Course Deviation Indicator
CNS	Central nervous system
DA	Decision Altitude
DH	Decision Height
DME	Distance Measuring Equipment
EASA	European Aviation Safety Agency
EEG	Electroencephalogram
EFIS	Electronic Flight Information System
EKG	Electrocardiogram
FAA	Federal Aviation Administration
FAF	Final Approach Fix
FL	Flight level

FNPT	Flight Navigation and Procedures Trainer
FRM	Fatigue Risk Management
FRMS	Fatigue Risk Management System
FTL	Flight Time Limitations
FTO	Flight Training Organization
FTS CTU	ČVUT Faculty of Transportation of Czech Technical University in Prague
GPS	Global Positioning System
HR	Heart Rate
HRV	Heart Rate Variability
HSI	Horizontal Situation Indicator
IAC	Instrument Approach Chart
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IFR	Instrument Flight Rules
ILS	Instrument Landing System
IMC	Instrument meteorological conditions
LOC	Localizer
LT	Local Time
NASA	National Aeronautics and Space Administration (USA)
NDB	Non-Directional Beacon
NOTAM	Notice to Airmen
NREM	Non-Rapid Eye Movement
NS	Nervous System
NTLx	NASA Task Load Index

NTSB	National Transportation Safety Board (USA)
PA	Precision Approach
PNS	Parasympathetic Nervous System
PPL	Private Pilot License
PSD	Power Spectral Density
QRH	Quick Reference Handbook
REM	Rapid Eyes Movements
SEP	Single-Engine Piston
SID	Standard Instrument Departure
SMS	Safety Management System
SNS	Sympathetic Nervous System
SPIC	Student Pilot-in-Command
STAR	Standard Terminal Arrival
VFR	Visual Flight Rules
VMC	Visual Meteorological Conditions
VOR	VHF Omnidirectional Radio Range

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1 Introduction

Most of the accidents in the early years of aeronautics occurred as a result of technical problems in airplanes [1]. Together with the technological developments and the production of turbo-jet engines beginning from the 1950s, which have allowed to design safer and reliable planes, there has been a significant decrease in the number of incidents and accidents caused by technical problems, marking important progress in-flight safety [1,2]. As problems with aircraft structure and systems have begun reducing, the primary attention was focused on defining and eliminating other causes that might affect flight safety. As a result of enhanced reliance on aircraft and flying devices brought by technological developments, preventing human error-caused accidents became a top objective of International aviation bodies such as the International Civil Aviation Organization (ICAO) and European Civil Aviation Agency (EASA).

Although the basic rules and principles of aeronautics have remained the same, more responsibilities have been added to the pilots' mission, converting pilots from workers using their mind and body, into the complex system managers. As flight deck automation advanced, new systems to assist pilots during flights have been developed, and new equipments such as autopilots, communication and navigation instruments, approach & landing systems, and avionics systems were adjusted to the modern glass cockpit environment in order to decrease the workload of a pilot, therefore, reducing human error-caused accidents [3]. On the other hand, if we consider a usual short-haul airline pilot who flies four legs up to eight legs during the flying season to the airline pilot in the 1970s who used to make approximately one leg per day; more workload, procedural responsibilities, and stress levels gradually were added to the pilots' daily duties.

Even though there have been great technological advancements in terms of engineering and technology-wise in the aeronautical industry in the last couple of decades, yet there has not been much improvement to the biological operators who daily use these advancements: the pilots. There does not seem to be a lot of difference between today's pilots and World War 2 pilots in terms of human factors since today's pilots still are dependent on using their basic sensation skills (seeing, hearing, touching, balancing, smelling, tasting), moreover, still, both of those pilots are biological mechanisms who are vulnerable to external elements such as stress, tiredness, emotional incompatibility, sleep deprivation, jet lag, long hours of work, with all of these aspects combined so-called as "pilot fatigue" [3,4,5].

At the early stages of the aviation industry, there was a general perception that the pilots were the only people influencing the performance of the single-pilot flight operations [3]. However, it should also be considered that not only the flier himself/herself; however, any person who assists in flight can have personal weaknesses and deficiencies. Human skill, reflex and abilities, level of knowledge, intelligence and reasoning, education and experience, excitement and emotionality, attention, fatigue, stress, personality structure, health, etc. all these factors affect flight safety in various ways [6,7]. The pilots are the crucial element in this complex system who are supposed to recognize and be able to eliminate the safety risks that are created by every element of the operational chain. Whenever a healthy functioning pilot is taken out of this system, the probability of catastrophic accidents becomes inevitable [8].

When it comes to ensuring successful flight operations, analysis of accident and failure results provide us important clues. In Figure 1, the main causes of accidents between 1959–1989 are given. It can be observed that more than 70% of the accidents that happened during the 30-year interval between 1959 to 1989 were caused by pilot error [2]. Therefore, it is crucial to define the factors that surround and lead to pilot errors and to analyze what can be done to minimize these errors to ensure maximum flight safety and efficiency on a day to day flight operations.

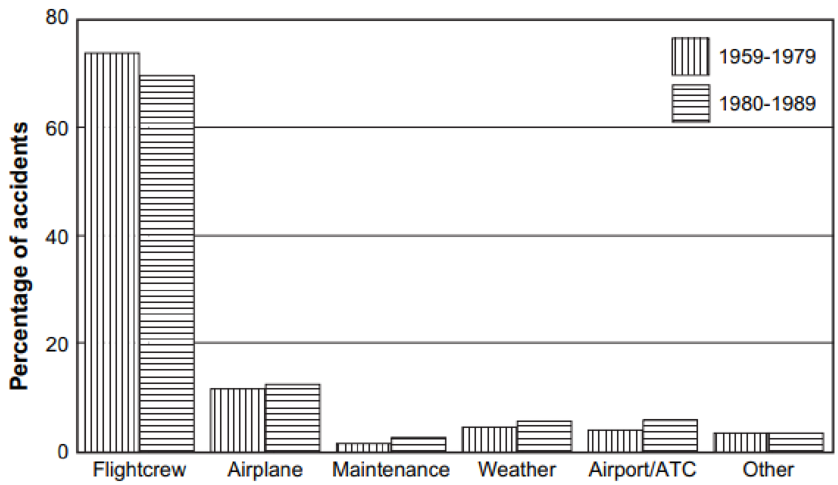

Figure 1: Primary causes of hull loss accidents (excluding military and sabotage): worldwide commercial jet fleet, 1959–1989 [9].

In aviation, the study of the human factors is becoming a multidisciplinary science, and it covers all aspects of the interaction between pilot and his surrounding environment: Decision making and other cognitive processes; cockpit and instruments; communications and software; maps, charts, aircraft operations manuals, checklists, e.g… [6,7]. When there is any type of air operation, there will always be a possibility of human error, and when subjected to stressful situations and/or work overload, more specifically monotonous work or underload, the probability of the occurrence of an error is even greater [10].

According to Boeing's statistics, 80% of the accidents in the early stages of aviation were caused due to machine error (equipment failures) and 20% due to human error (pilots, air traffic controllers, mechanics, etc.); however, that ratio has reversed with the beginning of the human factors era since 1970, 80% being human-error caused accidents and only 20% due to mechanical issues, citing pilot error as the root cause of an aviation accident [2]. The progress of technology and the implementation of new engineering techniques and processes tend to reduce the number of accidents caused by the machine, whereas increasing proportionally the percentage of those caused by flight crew [1,2]. This is because technological progress has not been matched by an equivalent growth in the area of human sciences. Or rather, there is still a lack of understanding of the mechanisms that lead to human error.

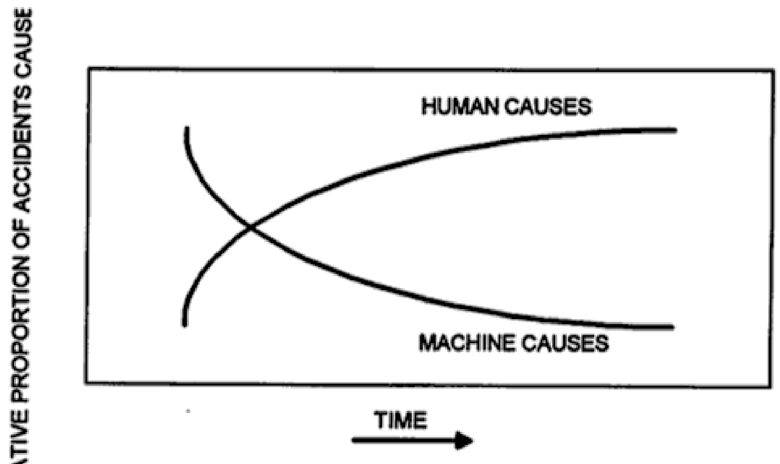

Figure 2. Changes in accident causal factors over time. (International Civil Aviation Organization, 1984)

Figure 2: Changes in accident causal factors over time. (ICAO, 1984) [1].

Although the human element is the most adaptable component of the aviation system, it is influenced by many factors that will affect flight performance such as fatigue, sleep deprivation, health, stress, and others that affect integrity and well-being [11]. Other external factors, when assuming extreme or abnormal values, also affect performance, including those caused by environmental restrictions such as temperature, noise, humidity, light, vibration, or due to functional restrictions such as working hours and responsibilities of the job [3,11].

In this work, physiological factors that lead to degradation of the pilot performance and induce pilot fatigue will be analyzed by evaluating the recorded heart rate activities from the measurements that were conducted on the fatigued pilots in simulated flight conditions.The results of these measurements lead to a method that will be able to evaluate fatigue in terms of the most significant indices of Heart Rate Variability (HRV) analysis. Despite the relative evidence of the robustness of some parameters of HRV analysis, there is unfortunately no consensus on the most accurate parameters to use in the current state of the art [12,13,14,15,16]. From a practical point of view, the absence of a clear and precise consensus on the HRV parameters leads to confusion and makes any rational comparison of similar studies difficult.

In order to illustrate our point: even though there is currently no norm that would determine the extent of mental stress solely based on LF/HF ratio; evaluation of stress using only this HRV parameter is utilized in many pilot fatigue related studies [12,17,18]. Whereas, in some others, the three of the most common SDNN,RMSSD,LF/HF ratio HRV indices are considered to assess pilot fatigue [13]. In a different study that combines objective and subjective measurements of pilot fatigue by using heart rate variability and NASA-

Task Load Index; LF/HF, SD1, SDNN indices are discussed during workload analysis [19]. There are also studies done which claim to show mental workload and fatigue experienced by pilots only by analyzing the amplitudes of maximum heart rate and minimum heart rate results (HRmax-HRmin) [14]. While some other studies found it necessary to analyze the values of many HRV parameters all together for the analysis such as: RR, SDNN, SD1, SD2, LF+HF, LF/HF, LFnu, HFnu [15]. Therefore, it would be interesting to ask why many researchers insist on publishing the results of each HRV marker at risk of presenting the same information several times and making the content confusing to the reader who will be overwhelmed by all these results without necessarily being able to isolate the causes and to attribute the effects on each of the indices studied.

It seems that proposing a list of the most significant parameters to the scientific community would tremendously help to strengthen hypotheses initially formulated by demonstrating the existence of a link not only with the overall HRV but also with a multitude of underlying indices. Conclusively, the fact that focusing on the analysis of a single index makes it possible to better target the underlying mechanisms that modulate it. Therefore, our purpose in this work is to come up with the global set of indices that provide the most accurate results which would be applicable to any research that deals with evaluating fatigue in terms of heart activity.

For the purposes of measurement, eight subjects were selected to participate in the 24-hour analysis. During the course, they gradually completed eight flights, and their performances were recorded at the flight simulator instructor station. Flight diagrams were designed so that the pilots' performances in individuals are comparable. Flights matched requirements and procedures for Instrument Flight Rules (IFR) flights, and each flight was terminated by a precision approach. Appropriate statistical and analytical methods were used to evaluate the data obtained.

Due to irregular flight roasters that are published according to Airlines' operational advantages rather than making allowances for proper rest of pilots; uncertain day and night shifts, even the possibility of being called back while in rest period due to the strict airline policies; fatigue is unfortunately fastly becoming a norm for nowadays airline flight crews. With the efforts to contribute solving pilot fatigue problem in the commercial aviation industry,this bachelor thesis will answer the following research questions:

1. How fatigue proceeds with flight time, what are the signs of fatigue on HRV indices, and what are the most significant parameters of HRV analysis that could be used globally for any pilot fatigue related research?
2. How can a fatigued flight crew member be excluded from the act of flying based on values of those HRV indices?

In light of these research questions, the hypothesis**:** “ pVLF index of the frequency domain and time-frequency domain analysis and nHF parameter of frequency-domain analysis of HRV corresponds to the most important indices” will be tested in this research.

2 Theoretical foundations of the work

For the purposes of measurement, it was necessary to induce fatigue in the subjects. One of the simplest ways to induce fatigue is to disrupt the normal daily rhythm of sleep and cause distributions in the circadian cycle [3,10,20]. Due to the cockpit environment, the challenges of the pilot profession and the needs of the measurement, this option seemed appropriate. Therefore, firstly it is necessary to define a theoretical concept of fatigue, its occurrence,possible consequences and existing measurement methods. It is also important to approach the process of sleep and stress and their effect on pilot performance.

2.1 Fatigue in aviation

In today's commercial aviation operations, it is expected that the flight crew is forced to extend their working time beyond scheduled due to various reasons such as: the lack of specialized personnel, delays, the various stages of flight, flight planning, and aeronautical maintenance activities [1]. Therefore, the pilots may encounter adverse aspects such as the unpredictability of working hours, interruptions in circadian rhythms, jet lag, sleep deprivation, and long duty time periods, which may expose them to fatigue. The impacts of fatigue on our ability to work safely impair a range of cognitive skills, including: situational awareness, reaction time, memory, decision making, and communication [3,21].

Fatigue is defined by ICAO as "A physiological state of reduced mental or physical performance capability resulting from sleep loss or extended wakefulness, circadian phase, or workload (mental and/or physical activity) that can impair a crew member's alertness and ability to safely operate an aircraft or perform safety-related duties" [22]. The fatigue phenomenon is responsible for the reduction of work skills, and impaired alertness due to long working hours, physical and mental exhaustion. All of these effects on pilots pose a direct threat to operational flight safety [8,20].

When a subject is fatigued, it could indicate a wide variety of conditions, including respiratory, cardiovascular, endocrine, gastrointestinal, hematological, infectious, neurological, and musculoskeletal diseases, affective disorders, sleep disturbances, and cancer [23]. Although, since it has multifactorial causes, fatigue sometimes cannot be easily diagnosable. Nevertheless, it has been found to be related to musculoskeletal diseases in 19% of the subjects , psychological and social problems in 16.5% of the subjects, neurological problems in 6.7% of the subjects and the alterations of the sleep cycle in 1.9% of the subjects [24]. In the same study, it was found that 50% of those fatigued subjects were suffering from anxiety in 61.1%, sleep cycle disturbances in 65% and depressive symptoms in 24.1% [24]. However, fatigue can also be a symptom of a disease caused by a virus that weakens the immune system [23].

Moreover, because the onset of fatigue is usually slow and unnoticed, there is a risk that the pilot will not realize the decline of his performance and capabilities [3].Most people know the definition of fatigue as tiredness; however, from an operational and more precise point of view, it could be defined as the condition characterized by the discomfort generated to perform a job, in the reduction of efficiency, the loss or difficulty in responding to stimuli (reaction time), and generally, is accompanied by a feeling of tiredness. However, this approach to fatigue, the main cause of which is represented by sleep debt or jet lag syndrome, is incomplete. Fatigue can indeed appear in pilots who do not previously have any sleep deficits and showing a high level of arousal but subject to intense activity [3]. The brain activation that will characterize such a level of awakening or overexcitement can be concomitant with a deterioration in performance, transformed into a sustained attention disorder, and, at the end of the working day, into difficulties falling asleep.

Fatigue has been identified as a contributing factor in accidents within a wide range of investigations, where a relationship has been found between tired pilots and the probability of poor performance and their respective actions [5]. According to the surveys gathered by European Cockpit Association between 2010 and 2012, over 50% of surveyed pilots from different European countries (Austria, Denmark, France, Germany, the Netherlands, Norway, Sweden, and Britain) have experienced fatigue at some point of their career that caused significant degradation of their flying performance [25].

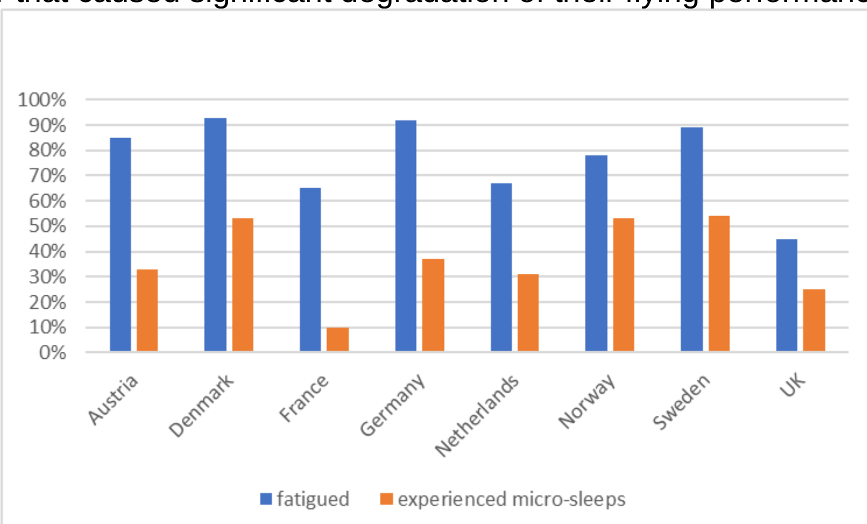

Figure 3: Percentage of pilot fatigue and dozing off or microsleep episodes [25].

In 2006, Britain carried out a study where the prevalence of fatigue in pilots during flight activities was 75% and the pilots reported that the feeling of fatigue had reached higher levels compared to previous years by 81% [21]. It was also found that low-cost airline pilots experience fatigue more frequently [21].

Another pilot fatigue survey that was conducted on 697 airline pilots who had 3/3/7 and 7/7 duty schedules in 2010 revealed that 84% of them had been fatigued at some point in their pilot career to a degree that had affected their flying performance, 28% reported they unexpectedly fell asleep during a flight, and they would prefer to sleep before duty rather than during the shift in order to avoid sleep inertia [26]. Additionally, it was also found out that the pilots have suffered the effects of fatigue the most during the flight phases of enroute flight, preflight planning and approach or landing [26].

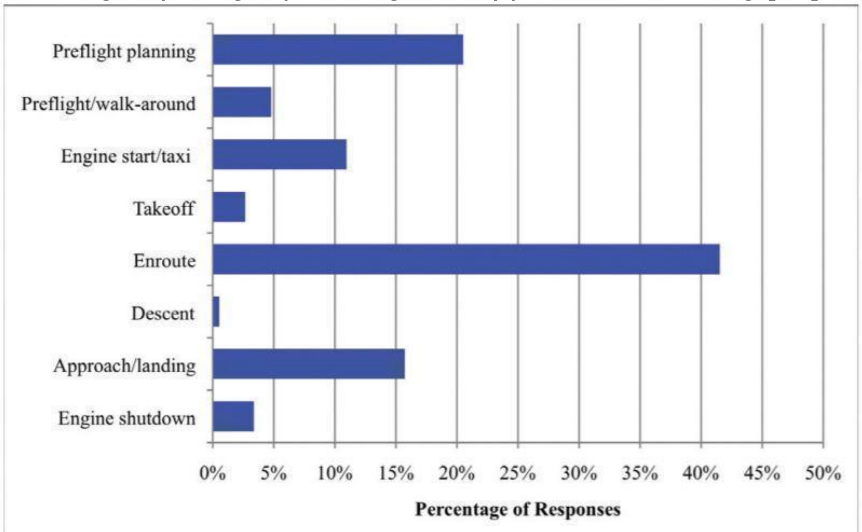

Figure 4: Different flight phases affected by fatigue [26].

In the same survey, micro-physiological events also have been recorded during the critical phases of the flight, the main event being micro-sleep, which is the sleep episode that can last for fractions of a second up to 30 seconds where the person loses connection with the environment [26]. In a different study, 87% of pilots experienced at least one micro-sleep greater than five seconds, and on average, pilots experienced six micro-sleep during the last 90 minutes of a flight [27]. In addition to micro-sleep, some pilots have admitted to falling asleep in the cockpit [27]. Similarly, in a study that was done by NASA in 1999, 80% of pilots have admitted unconsciously falling asleep at some point during flight [4].

Two basic types of fatigue can be distinguished, mental, and physical fatigue [6]. It is also possible to classify fatigue in terms of duration of it as short-term and chronic fatigue (long-term fatigue) [6]. The origin of physical fatigue is muscle work. Human cells can produce adenosine triphosphate (ATP), which is responsible for storing and releasing energy, both aerobically or anaerobically, depending on whether oxygen is available. When there is a lack of oxygen (anaerobic), the ATP is produced by using energy reserves (glucose) through cellular respiration, and carbon dioxide is released as an end product. This metabolic process, which generates energy, is referred to as anaerobic glycolysis [6]. However, energy production in this way is less efficient than with sufficient muscle oxygenation because the human body may not have a sufficient supply of oxygen since oxygen cannot be stocked in the body as good as blood sugar [6]. The bone marrow could be considered as a reservoir, but even so, only blood circulation is considered to provide an oxygen reservoir [7]. Thus, muscle work is typically associated with increased oxygen consumption besides an increase in tidal volume and respiratory rate [6].

Manifestations of physical fatigue include sudden pain, stiffness of skeletal muscles, cramps, loss of speed, or inability to do coordinated movements [6,7]. In extreme cases, it can be manifested by trembling of the hands and eyelids, the uncertainty of movement, feeling faint, general nausea, or rapid blinks of eyes [23]. Thus, physical fatigue appears to be a general weakness and exhaustion.

Mental fatigue depends on the induced mental workload and originates in the brain, and its first symptoms appear when the energy reserves in the brain are depleted [28]. It can often be diagnosed by exhaustion and sleepiness. Other manifestations include loss of concentration, impaired decision-making, memory impairment, or long response time[3,5,10,21]. Furthermore, mental workload enforces an increase in oxygen consumption which is attributed to the involvement of muscles and other parts of the body during concentration [6]. Therefore, mental fatigue may also be related to muscle tone. It's not unusual for mental and physical fatigue to occur together and to be related to each other. This typically occurs under monotonic and long-lasting loads without the possibility of rest [28,29].

In a study that proposes a fatigue model as a countermeasure for airline pilots, it was verified on 929 airline pilots that fatigue is influenced by 7 independent variables: flight direction, crew scheduling, partnership, aircraft environment, job assignment, ethnic difference, and hotel environment [30]. All these variables have an effect on physical and metal fatigue of pilots, as well as on their ability to have a proper rest [30].

Short-term fatigue is part of everyday life. Its onset is often associated with insufficient sleep and strenuous physical or mental activity. In aviation, it is caused by imperfect crew planning, long shifts, and jet lag. When occurring, the symptoms should be treated by adequate rest and quality sleep [6]. Prevention can then be with ,for example, sufficient healthy exercise and a balanced diet [6].

Chronic fatigue, also known as long-term fatigue, arises as a result of insufficient rest between different states of short-term fatigue. Other causes can be lack of exercise or too much mental or physical workload [6]. Typically, the problems at home, at work, or financial problems can mitigate chronic fatigue. The starting point of chronic fatigue condition is an incapacity for work and long convalescence in the form of rest [6,23].

2.1.1 Fatigue in long-haul vs. short-haul flights

The studies support that the type of air operation, whether it is a short-haul (less than 6 hours) or a long-haul (more than 6 hours), affects the pilots differently [28,31]. The questionnaire done on a group of airline pilots revealed that the medium/short-haul pilots experience higher levels of physical and mental fatigue than their colleagues who fly long-haul flights [28]. This can be related to the fact that the short-haul pilots are exposed to more stress during the landing phase since they usually fly multiple legs in a day, whereas, long-haul pilots experience less stress since they only need to perform only one or two landings a day. In another group of pilots, symptoms of fatigue in 60% of long-haul pilots and 49% of short-haul pilots were shown as a decrease in alertness and attention, a lack of concentration, increase in response times and tendency to make small mistakes in calculation and interpretation [31]. When they were fatigued, both of these groups of pilots reported that all the flying tasks seemed to be more difficult than usual [28,31].

Long-haul pilots indicated that approximately 60% experienced significant fatigue, at least once a week, which was associated with the work schedule ; and more than 96% reported that fatigue had interfered with their social activities in the last month [31]. Additionally, 59% of long-haul pilots reported that fatigue was accumulated mainly due to night flights, whereas 45% claimed it was due to experiencing jet lag [31]. Furthermore, regardless of type of operation, it was reported that 94% of the pilots in Indian Air Force feel the need to update training in sleep hygiene and the effects of fatigue, as well as the circadian rhythm [32].

When it comes to the short-haul operations, 53% of pilots suffered fatigue because of prolonged duty periods (4-5 leg multi-segment flights), while 41% suffered fatigue due to waking up early and abnormalities in their sleep cycle [31].

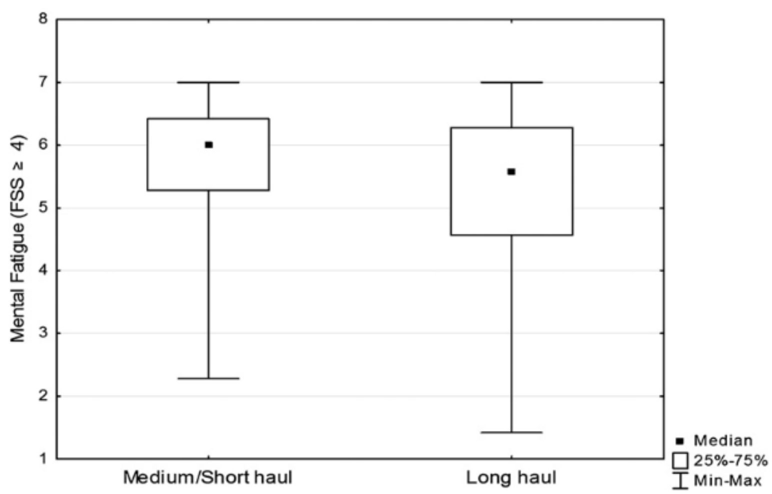

Figure 5: Comparison of mental fatigue for medium/short-haul and long-haul pilots [28].

2.2 Operational factors of fatigue

Multiple operational factors that pilots have to deal with in the commercial aviation industry have been related to a high probability of fatigue. The main ones are:

- Duty time: In a study carried out based on data from the FAA in 2002, it was found that the probability of an accident doubles when the duty time exceeds 10 hours and becomes 5.5 times when the duty time exceeds 13 hours [33]. Several articles evaluate long duty times as one of the most important fatigue contributors that could even be a predictor factor that leads to fatigued condition [3,5,11,21,27,28].
- The time of day when the flight is performed: There is a greater impact of fatigue on the flight crew when air operations are carried out during the circadian valleys and at night [3,5,6]. Fatigue has found to be present and progressively increasing more during night flights, manifesting its maximum peak between the hours 02:00 and 06:00 [6].

- The number of sectors flown (legs): There is a direct relationship between the number of legs performed by the pilot during the day and fatigue experienced [10,27,30]. Since each leg means 1 landing, as the number of legs that have to be performed by a pilot increases, the stress accumulated due to the responsibility to fly critical phases of flight (take-off/landing) would increase as well. Therefore, the crew enters a state of neurocognitive stress with increased number of legs [27].

- Rest period: It is crucial that pilots have enough time to recover from tiredness and the load of the day. Adequate rest schedule allows pilots to get a restful sleep and it decreases the probability of fatigue [5]. However, restful sleep time can be diminished by the psychological state of not being at home [5].

- Circadian rhythm: The aviation industry operates 24 hours a day and 7 days a week,therefore, there is a need to cover all schedules in shifts.This requires pilots to fly both in the day and the night operations, and often calling them early in the morning, which may lead to alterations in the quality and synchronization of sleep with the individual's circadian rhythm. Besides, especially long haul pilots are vulnerable to “Jet lag” because of crossing several time zones at once [6].

Overall, we can study these factors under 5 categories: Sleep, jet lag, duty time,stress and chemicals.

2.2.1 Sleep & circadian cycle

Sleep is the process during which recovery, the organization of mental processes and the arrangement of ideas takes place. It is a state of consciousness, and the amount of sleep required depends on the particular person and their age [7].The sleep credit/debit hypothesis suggests that for every hour of restful sleep, a person can stay awake and perform well for 2 hours [34]. That means that in a regular circadian rhythm, a person should stay awake for 16 hours and then needs 8 hours of restful sleep for regeneration, which is half of the time awake.

According to the sleep/wake credit/debit model [34]:

- 1 hour of sleep = 2 points of credit
- 1 hour of being awake = 1 point of debt
- maximum credit = 16 points (8hours of sleep) => it is not possible to “store” or “save” sleep for the future.

As an example, a pilot who has to be awake for his standard 16 hours will build up a sleep debit of 4 points. This will require him to sleep 2 more hours in the following sleep period, just as many hours as he has lost previously.

Sleep is also a physiological necessity like food and water, so nothing can compensate for the loss of sleep but the opportunity to recover it [5]. However, many times this is not possible due to long duty times or the type of air operations to be carried out as the total period of continuous wakefulness can easily reach 26-30 hours[3].Drug countermeasures, such as prescription or over-the-counter medications, can be an invaluable tool in maintaining alertness and performance for long periods of wakefulness or sleep restriction. Therefore, such prescriptions fail to address the major source of fatigue: insufficient sleep [4,5].

Many physiological processes in the human body function in cycles. The most common length of such a cycle is usually about 24 hours in humans and animals, which is called as circadian cycle or rhythm. It has a fundamental influence on the course of everyday life of humans and animals. Nevertheless, research in the field of the human factor proves that most people’s biological clocks work on a 25-hour cycle rather than a 24-hour one which is influenced by alternation of day and night, solar light, working hours, meal times, but also external factors such as noise [6].

Circadian rhythm controls, among other things, body temperature, heart rhythm, blood pressure and sensory adrenal activity [6]. Body temperature is the marker of the circadian rhythm [35]. It decreases in the evening, indicating that it is time to go to bed and facilitating the sleep, and increases early in the morning to wake up the organism [35].

The sleep itself is actually divided into several cycles, during which different types or stages of sleep occurs. In other words, sleep consists of several cycles, with each cycle including several “stages”. One sleep cycle lasts approximately 90 minutes whereas the proportions of the single stages within one 90-minute-cycle can change [6].

There are 4 stages of “quiet sleep”, followed by 1 stage of Rapid Eye Movement (REM) sleep [6]:

- **Stage 1:** Light sleep - this is the period of normal transition between activity and sleep that lasts about 10 minutes. During this period eyes move slowly under the eyelids, and muscle activity slows down . It is easy to be woken during this stage [6].
- **Stage 2:** Early sleep - this stage lasts about 20 minutes. It is characterized by “sleep spindles” (periods where the brain is inhibiting processing to keep the sleeper in a tranquil state). During this stage, muscular activity as measured by electromyography (EMG) lowers and the conscious awareness of the external environment disappears. This stage occupies 45% to 55% of the total sleep cycle [6].
- **Stage 3 & 4:** Orthodox (slow wave) sleep - it refreshes the body which is needed for tissue regeneration. This is a recurring sleep state during which rapid eye movements do not occur and dreaming does not occur. Also called NREM (non-REM) sleep, it allows for physical recovery of fatigue. Basically it has the function to recharge the individual’s batteries of physical energy, by resting the muscles and restoring the energy reserves (glucose) of the neurons [6].
- **Stage 5:** Paradoxical (REM) sleep - it refreshes the brain; strengthens and organizes the memory. It occurs about 70 to 90 minutes into the sleep cycle. A person usually has 3-5 REM episodes per night. It plays a crucial role in the memorization process and for emotional balance. During REM sleep the brain organizes memories and stimuli experienced during the previous day [6].

  In the first part of the sleep period, there are mostly NREM sleep cycles, but typically several instances of REM sleep stages occur during the entire sleeping time of a person (one in each 70-90 minutes of sleeping cycle). REM sleep becomes longer during the night (or the sleeping period) and typically increases significantly during the second 4 hours of an 8-hours sleep cycle [36]. REM sleep is characterized by extensive brain wave activity (if monitored by EEG the pattern would show similar brain wave activity as that of a person who is fully awake), rapid eye movement behind the eyelids, muscle twitches, and complex dreams [6].

  REM sleep is the phase in which our brain includes the new experience made the previous day with old knowledge. During this phase of sleep, the brain is highly active and vivid dreams are common, which help the brain organize its new data. In contrast to orthodox sleep, which is dedicated to regenerating physical health, the rates of breathing and heartbeat are higher and more variable in REM sleep [6].

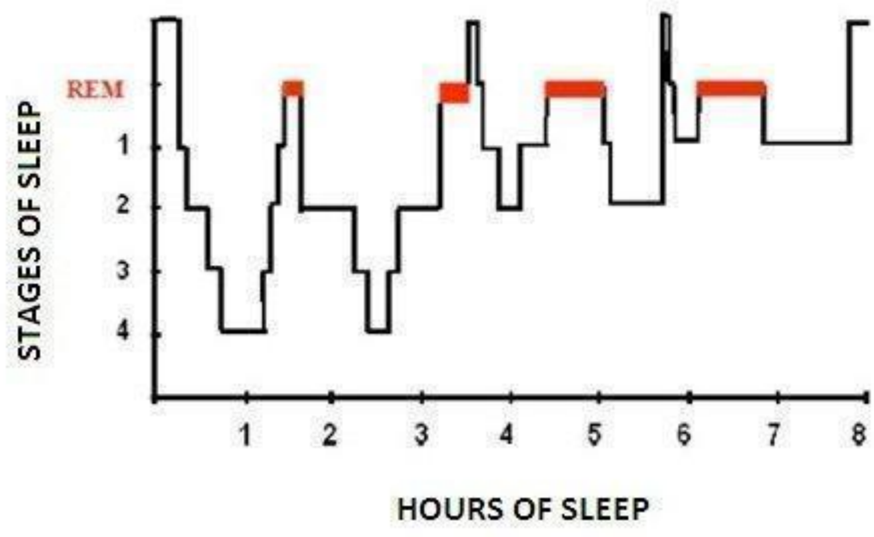

Figure 6: A sample hypnogram (electroencephalogram of sleep) showing sleep cycles characterized by increasing paradoxical (REM) sleep in a healthy young adult [37].

Alcohol consumption may decrease the time required to fall asleep. However, alcohol consumed within 1 hour of bedtime appears to disrupt the second half of the sleep period, which is mostly made of paradoxical sleep [37]. Alcohol causes humans to wake-up during dreams, interrupting the paradoxical (REM) sleep, leading to poor regeneration of the brain and mental functions [37].

The circadian cycle is governed by body temperature. Sleep is facilitated by a decrease in the body temperature, which occurs around 22:00, while waking-up is naturally caused by an increase in the body core temperature around 06:00. Within 24 hours body temperature normally ranges from 36.1 ° C to 37.4 ° C (see Figure 7) [35]. Therefore, drowsiness and the need for sleep are directly related to body temperature.

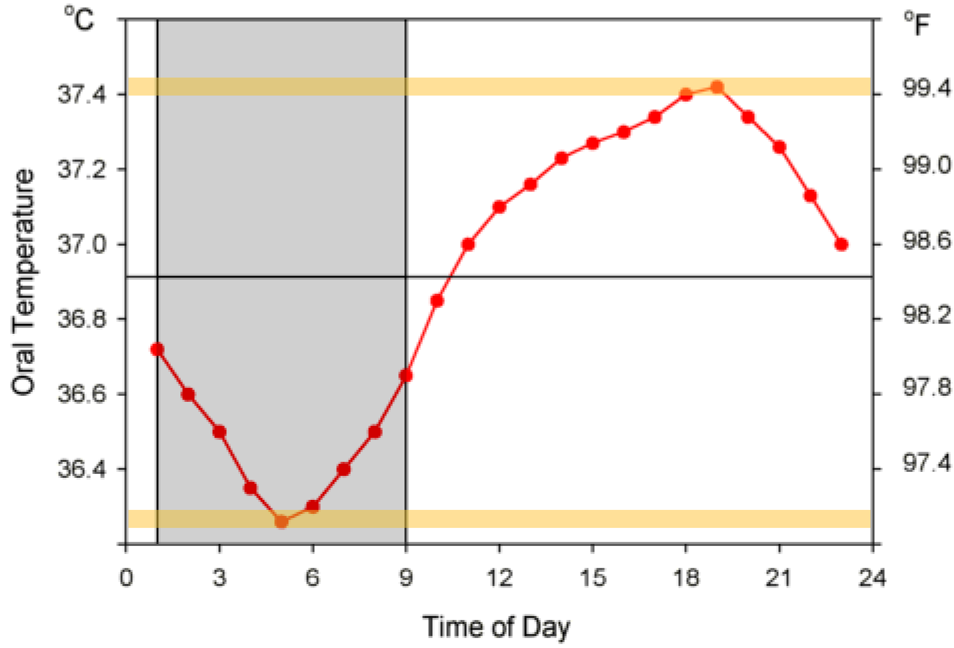

Figure 7: Daily variation of body temperature [35].

Therefore, it's not just enough sleep that matters but also the right timing and regularity. Even a very tired person can have trouble falling asleep throughout the day, because it is natural to sleep at night and be awake during the day. With the daily course of body temperature the performance of the individual is directly related [35]. Ability to solve simple tasks requiring short-term memory is followed by a curve of the daily course of body temperature (see Figure 7) [35]. With increasing body temperature, abilities improve and with decreasing, on the contrary, they degrade. Verbal reasoning and mental arithmetic skills peak around the afternoon [35].

Lack of sleep can have the same symptoms as drinking a small amount of alcohol [6]. It induces euphoric feelings, reaction time is prolonged and motor skills deteriorate. The decrease in pilot performance associated with lack of sleep is exacerbated by the high rate of flight altitude (cabin height which is around 8000ft). Although oxygen concentration in a parcel of air is the same as in the ground, which is 21%, partial pressure of oxygen decreases approximately linearly with height [6]. Therefore, even if there are small symptoms in the ground, when a fatigued pilot is forced to fly, since there is less oxygen intake, he can encounter amplified symptoms while flying.

2.2.1.1 Controlled in-flight rest

The most dangerous fatigue is when the pilot is just slightly tired, and he is not fully aware of it [38,39]. The performance decrease is there but since he does not realize it, he does not adjust the safety margins accordingly. To prevent tiredness and hypervigilance during flight, NASA recommends taking naps when it seems necessary [40]. In fact, many airlines recognize this and implement procedures called "controlled in-flight rest" or "operational nap". These procedures allow crew members to take short naps (up to 30 min), of course with additional measures to ensure maintenance of flight safety. 20 minutes is the recommended duration of the nap since it will give the benefit of 2 hours of "awake" potential [38,39]. But the pilots have to be aware that after waking-up even from such a short nap it may take up to 20 minutes to fully be operational again due to the sleep inertia phenomena [38,39].

Short naps, either before the start of operations, during the flight, or between stopovers, have shown that they are adequate as long as they are between 20 to 30 minutes, ideal time to counteract fatigue [38,39,40]. More than 30 minutes of nap time implies that the person enters deep phases of sleep and when waking up presents effects of sleep inertia, which causes a drop in performance and in turn a reduction in the waking state. The effects of sleep inertia can be severe, lasting from minutes to hours and, in addition, it can be accompanied by micro-sleep [26,27]. Therefore, taking naps as long as possible is recommended given the rule of thumb that at least 20 minutes is separated for recovering from sleep inertia.

It was also found out that having naps in the beginning of the deprivation period is better than taking it later because “it is always easier to prevent fatigue-induced decrements than it is to restore performance that has already deteriorated” [3]. Therefore, we can conclude that whenever the symptoms of fatigue begin to appear, placing naps should not be postponed. When fatigue is severe and complete sleep periods cannot be obtained, implementing the nap strategy can be immensely beneficial, reducing the tendency to sleep and helping to restore the impaired cognitive performance associated with fatigue. Even placing naps as short as 10 minutes has been found to help reduce subjective sleepiness and improve neuropsychological performance [38].

Napping can be done in assigned places on aircraft, where an environment is provided near the cabin, separate from the passenger cabin, providing comfort and opportunity to sleep.This strategy generates better sleep quality when it is carried out as early as possible during flight, that is, in the first part of the flight because it is possible to reduce the prolonged waking time and decrease the risk of sleep inertia [39]. In addition, cabin crew must be notified before starting an operational nap, in order for the cabin crew to verify the alert status of the pilot who remains in control of the aircraft. It is recommended that the nap should end 60 minutes prior to the start of the descent to avoid sleep inertia during approach and landing [38,39].

2.2.2 Jet lag

Jet lag, medically referred to as "desynchronosis" is a physiological condition which is a consequence of alterations to circadian rhythms. It is classified as one of the circadian rhythm sleep disorders. Jet lag results from rapid long-distance transmeridian (east-west or west-east) travel that crosses several time zones [6]. When traveling across a number of time zones, the body clock will be out of synchronization with the destination time, as it experiences daylight and darkness contrary to the rhythms to which it has grown accustomed. The body's natural pattern becomes upset, as the rhythms that dictate times for eating, sleeping, hormone regulation, and body temperature variations no longer correspond to the environment nor to each other in some cases. Because of the fact that the body cannot immediately realign these rhythms, it is called “jet-lagged”.

After a bad night's sleep, a person will be tired, but it will not cause a disturbance of his biological clock. This disturbance will occur when his circadian rhythm is not synchronized with the day/night alteration (in case of jet lag). For instance, a flight from Amsterdam to Johannesburg will not disturb the biological clock because the person remains in the same time zone. The flights that are crossing multiple time zones will disturb the biological clock, i.e. New York-Amsterdam.

When it comes to jet-lag it is known that most people’s biological clocks work on a 25-hour cycle rather than a 24-hour one [6]. Because of this, it is easier to adjust to the destination time when travelling in the westward direction (it extends the day). The rate of resynchronization is therefore faster for westbound flights (about 1 day per 1.5 hours of time shift) than for eastbound flights (1 day per 1 hour of time shift) [6].

2.2.3 Chemicals

Every drug has side effects, and many of them are incompatible with the pilot's duty. If a pilot is not sure about a prescribed drug, he should seek medical advice. The safest approach is to take no medication while flying except on the advice of the Authorized Medical Examiner (AME). Studies of aircraft accidents suggest that certain widely used medications have side effects that contribute to pilot error and hence to accidents [41,42]. They are normally considered incompatible with flying. Many unprescribed drugs used to threaten headaches. The commonly used cold or sleeping pills have a significant array of side-effects for pilots. The most critical side effects for pilots being the reduction in attention time and decreased perceptual awareness [3].

A study concentrating on fatigue in aviation alleges that the most commonly prescribed medicines by AME to recover pilots from either falling asleep, or to enforce sleep can sometimes lead to excessive alertness or drowsiness in flight crew which can lead to undesired effects [3]. The study also claims that non-prescription medications that often contains pseudoephedrine (CNS stimulant that generates alertness and makes falling asleep harder) and usual head-ache pills that contains 65 mg of caffeine per tablet, once taken the recommended dose (2 tablets), could easily interfere with the sleeping cycle[3].

Another fatigue countermeasure that is occasionally used by some commercial pilots is the use of caffeine gum that consists of 200 mg dosage. Because of its rapid absorption in 15 minutes and a elimination from the body in 5 hours, it would be recommended to use it in the last part of the flight with precaution [43].However, regular usage of caffeine gum has found to create tolerance, and would require the pilots to increase the dosage gradually to obtain the same effect,which is not acceptable [43]. The use of hypnotics has been limited in the United States Air Force, and remains controversial in civil aviation [43]. Despite the aforementioned, short half-life molecules such as modafinil are an option to use as sleep inducers, their prescription are made according to the evaluation of each particular case by AME.

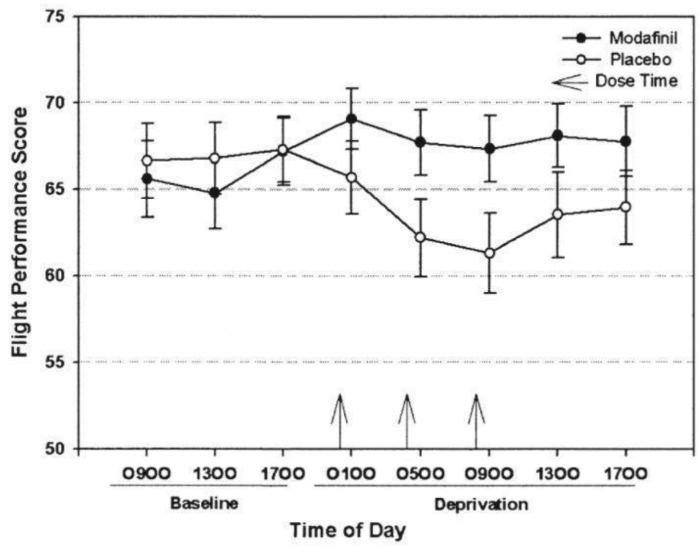

Figure 8: One of the most commonly used prescription medicines is modafinil which is effective for short term fatigue management [44].

Additionally, harmful aspects of recreational drugs, smoking and consuming alcohol is a well-known fact that contribute to the generation of fatigue [6,7,36]. EASA implements strict regulations and performs random controls to enforce the laws about this issue. The regulation prohibits the pilot to consume alcohol within 8 hours of performing aerial work providing that the blood alcohol concentration (BAC) does not exceed 0.02%, which is 0.2 grams of alcohol per litre of blood ; and the breath alcohol concentration (BrAC) does not exceed 90 micrograms of alcohol per litre of breath[45]. Therefore, for our measurements, we have selected subjects who do not use any kind of drugs, smoke or consume alcohol.

2.2.4 Stress

For commercial pilots it is almost a natural part of their self-image to be able to handle stress well. Working conditions and tasks have the common attributes of strong stressors: high responsibility, multiple workloads, time pressure, noise, a constant and intensely changing environment, to name but a few, are directly related to pilot profession.

If stress persists over a longer period of time, it depresses our productivity and threatens our health. Too much stress can trigger more than half of the most common diseases [46]. Extreme stress can cause panic and possibly even loss of motor skills [46].Therefore, pilots are continuously being exposed to and are vulnerable to stress in their daily life. Understanding the causes and developing effective methods to prevent or at least reduce stress have been a focus of aviation medicine researchers since the beginning of the commercial aviation era.

Stress also affects different types of air operations differently. Private pilots are not generally exposed to the same operational stressors as commercial pilots (long work days, circadian disruptions from flying at night or time zone changes, or forecast changes). However, they will still develop fatigue from a variety of other causes. Given the single-pilot flight operation and the relatively higher workload, they would be in danger (possibly even more) of being involved in an accident, just as much as a commercial team. Anyone who is fatigued will exhibit the same problems: drowsiness, difficulty concentrating, apathy, a feeling of isolation, annoyance, increased reaction time to stimuli, reduced high-level mental functioning, decreased alertness, memory problems, task fixation, and increased errors while tasks are running [5,46]. It is not good that this happens to a pilot if there is no other person on the plane who can help.

Like all people, pilots also bring the stress of their non-professional life to the cockpit, which adds an additional stress to the act of flying. In terms of aviation, stress plays a central role in crew resource management. It directly affects all the crucial processes in the cockpit such as decision making, information processing, and communication with other crew members [6,46]. Especially decision making is one of the greatest sources of stress in the cockpit. The responsibility to make appropriate decisions under the given circumstances is one of the main triggers for mental stress. If the time pressure is too great, the willingness to make risky decisions increases which leads to disregarding of the prescribed procedures [47]. The crew is then very much quickly in the so-called poor judgment chain [46].One of the signs of high stress on the crew is the decrease in the verbal communication.The breakdown of communication is one of the most common reasons in the causal chain leading to the accident [46].

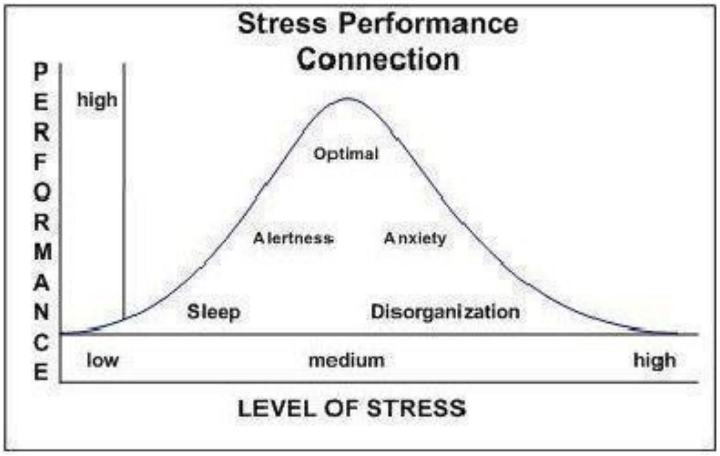

Figure 9: Yerkes-Dodson Law is modeled as a U-shaped curve [47].

Yerkes-Dodson law states that a reasonable level of stress is even healthy and increases performance since it assures an optimal level of alertness [47]. When it comes to how to prevent an unhealthy amount of stress, the best answer seems to be maintaining both a physically and mentally healthy lifestyle, getting quality rest and persisting a conflict-free attitude both in professional and personal life [3,6,7].

In the early years of aviation, stress condition in pilots was mainly induced due to physiological stressors in nature, i.e. vibration, noise, temperature, turbulence, etc. At present, it is necessary to focus on new sources of stressors, which may be lack of sleep, irregular sleep cycle, night flights or irregular working hours. Mental stress can be assessed in two different ways. Psychological methods are based on an interview or questionnaire completion such as the NASA Task Load Index. However, these measurement approaches provide only a subjective evaluation, which takes place after the completion of the event and can therefore be misleading. On the second hand, there are physiological studies that objectively assess the burden of changes in the human body according to measured physiological parameters, such as heart rate variability as we studied in this work.

2.2.5 Duty time

Airline operators and pilots are required to comply with legal requirements for maximum duty time and minimum rest time. The duration of this time is defined under the regulation EASA FTL, ORO.FTL.210, Flight Times and Duty Periods. According to the regulation [48] :

(a) The total duty periods to which a crew member may be assigned shall not exceed:

(1) 60 duty hours in any 7 consecutive days;

(2) 110 duty hours in any 14 consecutive days; and

(3) 190 duty hours in any 28 consecutive days, spread as evenly as practicable throughout that period.

(b) The total flight time of the sectors on which an individual crew member is assigned as an operating crew member shall not exceed:

(1) 100 hours of flight time in any 28 consecutive days;

(2) 900 hours of flight time in any calendar year;

and (3) 1000 hours of flight time in any 12 consecutive calendar months.

***(c) Post-flight duty shall count as a duty period.** The operator shall specify in its operations manual the minimum time period for post-flight duties.*

where "Block flight time" means the time between the first movement of an aircraft on departure parking space in order to take off to a stop at the designated parking space and after the stop of all engines or propellers [48].

However, airlines today prefer to plan crews on the edge of legislation where it can happen, that the maximum crew time could be exceeded due to unforeseeable circumstances in duty. Therefore, there is also a regulation setting the options of the crew in case the extension of duty time is inevitable due to various reasons. It says that [49]:

Unforeseen circumstances in flight operations — commander's discretion:

(1) The conditions to modify the limits on flight duty, duty and rest periods by the commander in the case of unforeseen circumstances in flight operations, which start at or after the reporting time, shall comply with the following:

(i) the maximum daily FDP which results after applying points (b) and (e) of point ORO.FTL.205 or point ORO.FTL.220 may not be increased by more than 2 hours unless the flight crew has been augmented, in which case the maximum flight duty period may be increased by not more than 3 hours;

(ii) if on the final sector within an FDP the allowed increase is exceeded because of unforeseen circumstances after take-off, the flight may continue to the planned destination or alternate aerodrome; and (

iii) the rest period following the FDP may be reduced but can never be less than 10 hours.

(2) In case of unforeseen circumstances which could lead to severe fatigue, the commander shall reduce the actual flight duty period [49].

Although a "long-haul flight" is defined as a flight which lasts 6 hours or more, and is often associated with multiple pilot operations; according to the legislation a third pilot is mandatory after exceeding the flight time of 8 hours. Additionally, two complete crews (a total of 4 pilots) are required for long-haul flights of more than 12 hours, in which the flight time does not exceed 18 hours [49]. Such a case is called a split duty. In order to organize split duty operations, an operator must ensure the reservation of a resting space for the crew where pilots can adequately rest [49].

For operating in compliance with split duty regulations, this reserved space should only be accessible by another crew member, and it should be in a different section than the passenger compartment [49]. Each crew member should have at least an adjustable seat or directly a bed on board the plane [49]. For reinforced crew (i.e. one additional pilot) the total continuous rest period must not be less than 3 hours, besides, the duty time must not exceed 16 hours [49]. The total length of service rule still applies to split duties; The total time in service before and after rest may not exceed 12 hours [49].It is still true that this period can also be extended by "unforeseen circumstances" 2-3 hours more according to the regulation [49].

Start of FDP at reference time	**Sectors**								
06:00 -13:29	**1-2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
13:30 – 13:59	13:00	12:30	12:00	11:30	11:00	10:30	10:00	9:30	9:00
14:00 – 14:29	12:45	12:15	11:45	11:15	10:45	10:15	9:45	9:15	9:00
14:30 – 14:59	12:15	11:45	11:15	10:45	10:15	9:45	9:15	9:00	9:00
15:00 – 15:29	12:00	11:30	11:00	10:30	10:00	9:30	9:00	9:00	9:00
15:30 – 15:59	11:45	11:15	10:45	10:15	9:45	9:15	9:00	9:00	9:00
16:00 – 16:29	11:30	11:00	10:30	10:00	9:30	9:00	9:00	9:00	9:00
16:30 – 16:59	11:15	10:45	10:15	9:45	9:15	9:00	9:00	9:00	9:00
17:00 – 04:59	11:00	10:30	10:00	9:30	9:00	9:00	9:00	9:00	9:00
05:00 – 05:14	12:00	11:30	11:00	10:30	10:00	9:30	9:00	9:00	9:00
05:15 – 05:29	12:15	11:45	11:15	10:45	10:15	9:45	9:15	9:00	9:00
05:30 – 05:44	12:30	12:00	11:30	11:00	10:30	10:00	9:30	9:00	9:00
05:45 – 05:59	12:45	12:15	11:45	11:15	10:45	10:15	9:45	9:15	9:00

Table 1: Maximum daily Flight Duty Period (PDP) according to the number of sectors flown [50].

Above mentioned regulations that define maximum duty time and minimum rest time in several scenarios are one of the first countermeasures enforced by EASA and national civil aviation authorizations for prevention of fatigue. These regulations are even more advanced by the Fatigue Risk and Management System (FRMS) that was developed by ICAO as a means to continuously monitor and maintain related security risks with fatigue, based on scientific knowledge, principles and operational experience to ensure reasonable levels of vigilance [51].

2.2.6 Fatigue Risk Management System (FRMS)

ICAO deals with fatigue at international level. According to ICAO, the FRMS is a system guided by continuous monitoring and management of operational safety risks related to crew fatigue, and aims to ensure that they operate with a satisfactory alert level. It applies principles and processes of a Safety Management System (SMS) to manage the risks related to fatigue and, therefore, seeks to balance safety, productivity and costs [1,51]. Both SMS and FRMS depend on the safety culture of training personnel involved in the activity to identify and report hazards in the operation. In parallel, this model is based on scientific knowledge about fatigue and sleep, which has advanced a lot in the last decades, and also on the science of safety.

Basic principle of the FRMS system is the cooperation of the state, the operator and individuals with each other. The state defines a regulatory framework that should ensure the required level of safety. The operator is then responsible for properly planning the crews so that they are able to perform their task safely. Furthermore, the operator monitors and manages the risks of fatigue. The pilots in this chain of systems are responsible for their condition when entering the service, taking advantage of opportunities for rest and reporting occurrence of fatigue [1].

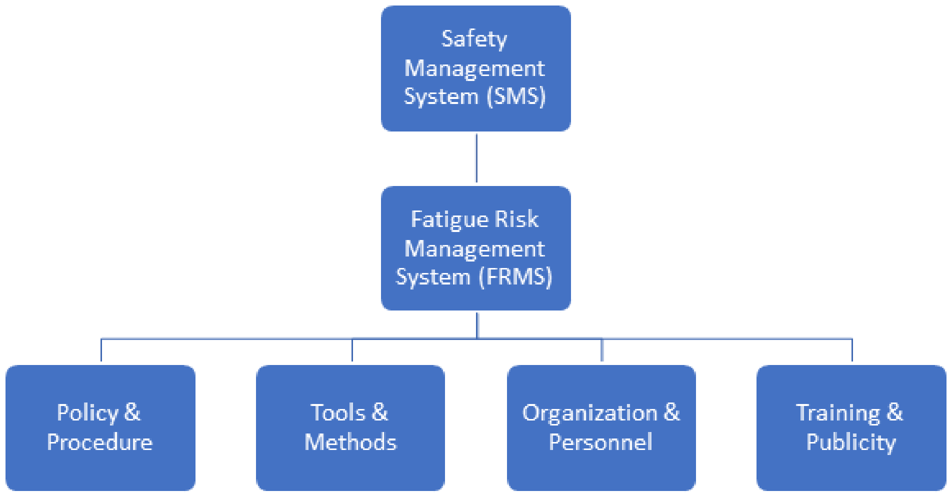

Figure 10: SMS and FRMS structure [52].

SMS Framework	FRMS Framework
Safety policy & objectives ● Management commitment and responsibility ● Safety accountabilities ● Appointment of key staff members ● Safety response planning ● SMS documentation	**FRMS policy & documentation** ● Management commitment ● FRMS accountabilities, responsibilities, and authorities ● FRMS objectives ● FRMS processes and procedures ● FRMS training records
Safety risk management ● Hazard identification ● Risk assessment and mitigation	**Fatigue risk management** ● Identification & assessment of fatigue-related risks ● Fatigue-related risk mitigation/controls ● Implementation ● Evaluation
Safety assurance ● Safety performance monitoring and measurement ● Management of charge ● Continuous improvement	**FRMS safety assurance** Monitor FRMS effectiveness ● Processes for managing change (to the operational/organization environment and/or to the FRMS itself) ● Continuous improvement of the FRMS
Safety promotion ● Training and education ● Safety communication	**FRMS promotion** ● Training programs ● FRMS communication plan

Table 2: Comparing SMS and FRMS components SMS [53]

Therefore, it can be said that, like SMS, FRMS depends on an efficient structure of security reports, company management's commitment to the tool, continuous monitoring process, a process of investigation of occurrences of security that aims to identify deficiencies rather than finding a culprit, sharing information and good practices, integrated staff training operational, effective implementation of *Standard Operating Procedures* (SOPs). Therefore, it is a commitment to continuous improvement. The document Doc 9966, Fatigue Risk Management Systems Manual for Regulators, deals with regulations and recommendations set by ICAO in order to prevent fatigue.

Finally, FRMS is today the most efficient tool for managing fatigue, since it is based on the application of scientific knowledge and principles to the management of risks associated with fatigue. It assures that within the limits of flight time and journey, the flight will be free of risks associated with fatigue, and implements a new ability to identify, and evaluate mitigation controls and strategies.

2.4 Measuring fatigue

In the concept of fatigue, its evaluation can be a complementary approach. Three types of assessment methods of mental effort and workload can be distinguished:

1. **Subjective or Psychological measurements** of the NASA Task Load indeX (TLX) type which takes into account 6 workload dimensions: mental demand, physical requirement,time pressure, performance, effort and level of frustration. This scale seems particularly suited to the aeronautical field [19].

   Furthermore, the subjective components of fatigue are assessed through analog questionnaires or scales. The principle of these scales is to ask the subject to assess their feeling of fatigue by writing a mark on a horizontal line separating two opposite adjectives, for example: tired-rested [19]. In addition to NASA TLX ,there are various tools to assess this component, in particular through biographical questionnaires such as those developed by Halmes and Rahe in 1967[54].These so-called "life events" scales allow us to understand the affective component exerted on a subject, often mentioned as an element contributing to increased manifestations of fatigue.

2. **Objective or Physiological measurements** of the evoked potential type, respiratory activity, cardiac frequency variability. The most used parameter for analysis is cardiac variability. It was proven during fatigue and its physiological effect works in particular that the power variations in the frequency band 0.06 Hz - 0.14 Hz reflect the amount of effort provided in a task that was performed by a pilot [13,14,15].

3. **Dual task methods** which consist in saturating the subject's working capacity by gradually adding tasks of various difficulties. The deterioration in performance reflects the intensity of the effort invested by the subject while performing the tasks [55]. Nonetheless, even though it was used in a study to demonstrate that psychomotor processes and attentional functions of astronauts are prone to disturbance during an 8-day space mission, this method of measuring is impractical for our purposes because in reality this is not the way fatigue is induced on pilots [55]. During our measurements our main goal is to detect fatigue while a pilot performs his tasks in an usual orderly routine and under normal circumstances rather than in an expedited manner. Furthermore, this kind of measuring type is not utilized in the literature which examines pilot fatigue, consequently, we will abandon this method here.

	Fatigue measurement methods	Main tool	Measurement target
Subjective measurements	Self-reporting questionnaire (psychological)	● Depression Scale ● Stress test ● Well-being scale ● Personality test	Self-report by scoring
Objective measurements	Biochemical inspection (hormonal)	● Endocrine activity ● Autonomic nerve activity	Cortisol levels, adrenaline levels, thyroid levels
	Physiological inspection	● Autonomic Nervous System (ANS) activity	Heart rate variability, blood pressure, brain wave activity, blood temperature, skin conductivity
	Awakening inspection	● Sensory motor boundary inspection	Reaction time for a visual stimuli (PVT)

Table 3: Tools for stress and fatigue evaluation.

For our purposes of measurement, we preferred to perform physiological types of measurements to be able to objectively evaluate the data.

2.4.1 Physiological indicators

As we have discussed in the last chapter, fatigue can develop from various sources. The important factor is not what causes fatigue, but the negative impact that fatigue has on the person and their ability to perform tasks. A long day of mental stimulation, like studying for a test or processing data for a report, can be just as exhausting as manual labor. Outcomes of these activities may feel different - a sore body rather than a headache and cloudy eyes - but the effect is the same, the inability to function normally. A fatigued condition of a subject affects every physiological aspect of his body differently. However, in general, we can say that fatigue tends to increase muscular and mental response time to a stimulus. We can generalize the consequences of fatigue in a subject in terms of physiological and psychomotor changes as in the table below.

Physiological changes	**Changes in psychomotor level**
↓ *Body temperature*	↓ *Memory*
↓ *Muscle strength*	↓ *Communication skills*
↓ *Binocular vision*	↓ *Eye tracking abilities*
↓ *Circulating blood volume*	↓ *Attention*
↓ *Muscle control and coordination*	↓ *Ability to cooperate*
↑ *Blood glucose*	↓ *Self judgement and awareness*
↑ *Pupillary response time to light*	↑ *Reaction time*
↑ *Visual accommodation time*	↑ *Irritability, anxiety*
↑ *Eye strain*	↑ *Error rate*
↑ *Cardiac frequency*	↑ *Omissions*

Table 4: Effects of fatigue on a subject in physiological and psychomotor level [3,6,20,56].

According to literature, fatigue can be measured objectively using the following ways:

- By observing eye movements (*Fixation duration, Saccade frequency, Blink latency , Blink duration , Pupil diameter)* [58];
- By monitoring heart activity using ECG *(Heart rate)* , by monitoring respiratory activities *(Respiration rate , Respiration depth)* [13,14,15];

- By testing the chemical changes in body *(Hormonal levels, Urinalysis, Blood pressure, Carbon dioxide in blood plasma)* [57];
- By monitoring brain wave activities using EEG [59];
- By measuring ration time to a visual stimulus by Psychomotor Vigilance Test (PVT) or psychomotor coordination using Motion Capture systems [64].

  All these various methods to measure fatigue have their own advantages and disadvantages.

Measuring hormonal changes relies on detecting several pathological states that are associated with fatigue such as hypothyroidism, renal failure, or anemia [57]. By taking blood samples, information about fluid and electrolyte status, renal function, liver function, and metabolic status are obtained [57]. Hemoglobin values are utilized to evaluate competence of oxygen carrying capabilities of body cells. Since normal thyroid levels are associated with healthy metabolic functioning and because thyroid pathology is associated with fatigue, obtaining thyroid measures are also used [57]. However, testing the chemical changes in the body is not a widely used approach for measuring fatigue during simulated or real flight conditions, since it would require interruption of flying tasks for getting blood and urine samples in constant intervals.

Utilizing eye-tracking measures is a relatively new approach in fatigue studies. Fatigue, stress, and hypoxia conditions all notably affect eye movements [58]. Visual tracking, saccadic velocity, and approximate entropy are among several metrics of fatigue indicators [58]. It was found that saccadic velocity can be used as a reliable biomarker for pilot fatigue studies, as its value decreases with sleep deprivation [58]. And, approximate entropy corresponds to performance decrements [58]. Fatigued condition of the subjects can be predicted by long eye closure rate and high blink amplitude [58]. Similarly, the presence of a stressor or a challenging situation can be determined by observing reduced eye closure rate than normal and short blink amplitude [58]. However, we could not use this approach of measuring since it requires a very sensitive equipment to track eye movements continuously.

Tracking brain wave activities for determining fatigue using EEG is a relatively contemporary method. This is accomplished by the spectral analysis of the EEG signal by observing the shifts in alpha, theta and beta power components (α, θ and β) which is considered as "a neural signature of cognitive fatigue" [59]. Studies reveal that when the pilots were kept awake between 23-26 hours, the fatigue caused by sleep deprivation could be observed on the theta and delta activities of the EEG signal collected during real or simulated flights without interfering with the aerial work [60,61]. Also, power components can also be used to determine the intensity of MWL. Theta activity was reported to increase during the segments of flight that requires the highest levels of cognitive processing, such as take-off and landing, and the reduction in the theta activity was observed during the phases of flight which requires more psychomotor coordination, such as touch and goes in VFR conditions and climbout in IFR conditions [60,61].There is a consensus among researchers working on this topic that EEG theta component shows increased values and EEG alpha component decreases with increased flying tasks or enforcing more demanding tasks [60,61,62,63]. On the other hand, it is still not certain that this method of pilot fatigue evaluation is a reliable method due to the complexity and difficulties in interpreting the brain wave activities [60]. Besides, there seems to be a lack of knowledge and a standard procedure to appraise pilot fatigue in terms of brain activity. Although the values of the ECG and EEG records made at the same measurements results in unique, but somehow similar conclusions, working on heart rate data is accepted to be a more decisive method for psychophysiological assessments of pilot fatigue [62,63].

Examining psychomotor coordination of our measurements to determine pilot fatigue was already done using Motion Capture systems. Based on the result, it was concluded that fatigue affects physical activity of the pilots during the measurements where the subjects experienced variable levels of fatigue during a total of 24-hours of sleep deprivation [64]. It was found that variability movement increased with increasing fatigue, just as mobility itself increased [64]. Furthermore, it has been proven that variability and mobility are associated with the circadian rhythm of humans and times of attenuation, these two parameters increase [64].

Therefore in this work,we preferred to use monitoring heart rate activity of the subjects since it is considered as the most reliable and widely used approach for objective type measurements of pilot fatigue in aviation medicine literature and due to our available equipment in the laboratory of human factors in aviation.

3 Evaluation of Heart Rate Variability (HRV)

3.1 Cardiac activity and HRV

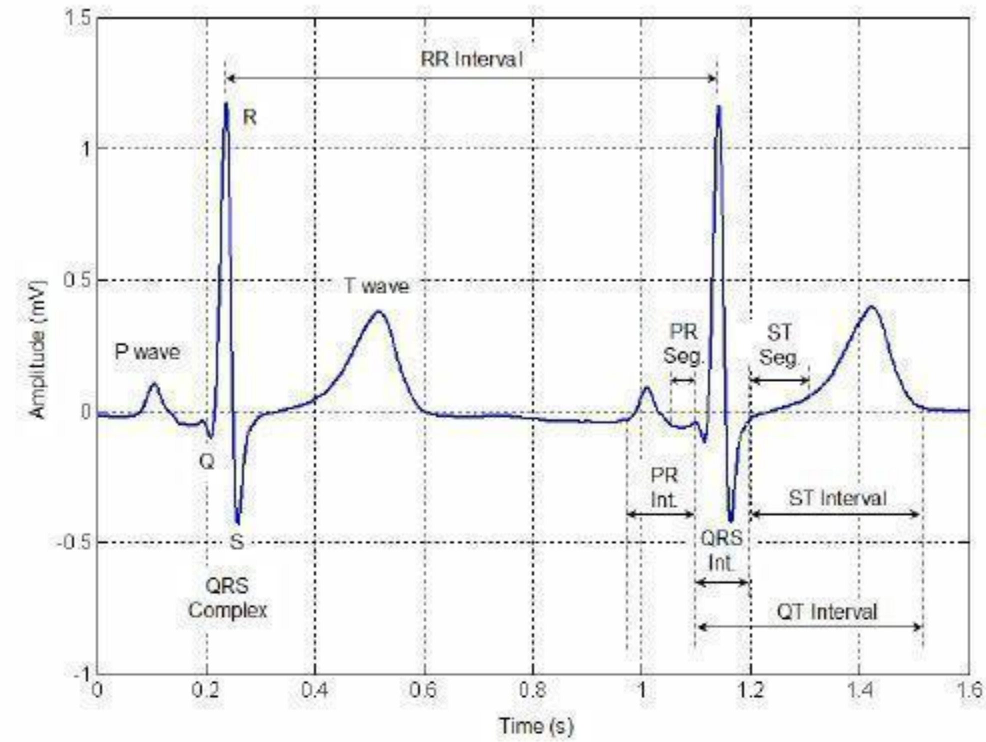

Figure 11: An example of an ECG wave, its segments and intervals [65].

Heart rate (HR) is defined as the number of beats the heart makes in a minute. While being a reliable parameter that is used to evaluate the heart activity and performance, it is an indicator of the intensity of the mental and physical workload exerted on a pilot [13,14,19]. HR recordings, or tachographs, are collected using a heart rate monitor or electrocardiogram (ECG). The transformation of this signal into a numeric sequence allows us to obtain the elementary values of the RR intervals of the QRS complex.

Heart rate has been probably the most widely used physiological parameter for pilot fatigue analysis [14,15,19]. It is not surprising that heart rate measuring is used often by researchers interested in behavioral responses because of its convenient measurability, cost efficiency, well documentability with unsophisticated equipment (ECG), and applicability on pilot subjects during actual and simulated flying conditions [66].

Electrocardiography is a technique for recording bioelectric currents generated by the heart muscles. The graphic representation of this recording is called an electrocardiogram as shown on the Figure 11. The term “ECG” is used interchangeably to refer to both the electrocardiogram and electrocardiography. It is used clinically to diagnose various diseases and in our case to detect occurrence of pilot fatigue and decrease in flying accuracy and performance.

The principle of ECG recording is that the potential difference is measured between two points diametrically opposed with respect to the heart, this signal being directly correlated with the displacement of the electrical impulse in cardiac muscle fibers. The ECG is necessary as a basic tool for HR measurement, essentially for two reasons: It allows us to easily acquire a signal by precisely placing electrodes on the subject's skin and to record the electrical signal obtained which is characterized by succession of the waves.

For each heartbeat ECG records 4 successive waves. Each pair of cavities (the atria and ventricles) has its own electrical signature on an ECG record as following:

1. The P wave: represents the electrical activity of the depolarization of the atria. It generates low amplitude compared to other waves, its duration varies between 80 and 100 ms, its maximum amplitude is 0.25mv [67].
2. The PQ segment: allows the atria to empty into the ventricles before the contraction of it [67].
3. The QRS complex: corresponds to ventricular depolarization; it is represented by a peak steep whose duration is around 0.1s, its amplitude varies between 0.5mv to 2mv [67].
4. The T wave: corresponds to the repolarization of the ventricular muscle [67].

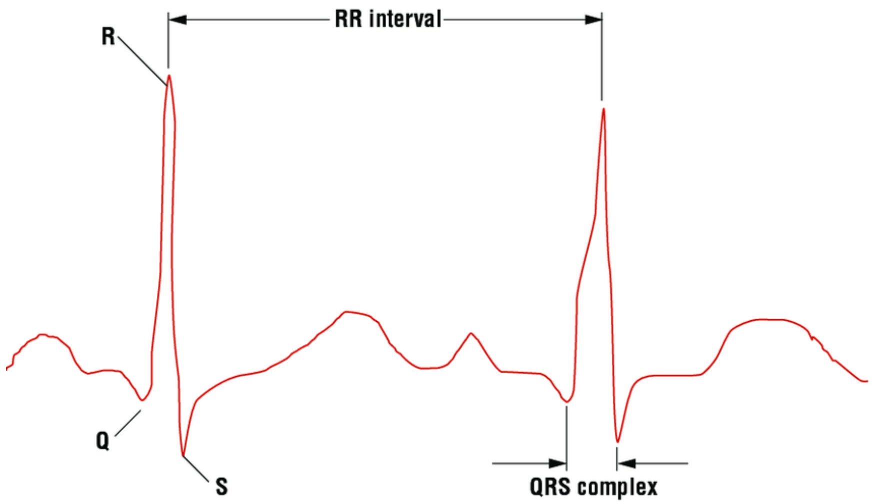

Figure 12: A QRS complex.The RR interval indicates the time between heartbeats [68].

The R peak allows a measurement of the time interval between two of these peaks (RR) and gives access to the heart revolution. The continuation of the RR intervals, allows us to evaluate the HR rhythm of a subject and its variability over time which is called as Heart Rate Variability (HRV) that is used to distinguish rest, fatigue and stress conditions experienced by a subject [13,14,15]. If the heartbeat was perfectly regular, the RR interval would be displayed as a constant signal. The figure 13 reveals that this is not correct and that the RR series are subject to significant fluctuations that are caused by the reaction of the subject to mental and physical loads. The figure displays the RR intervals extracted from an ECG signal that is used to calculate HRV and to determine cardiac vagal control [69].

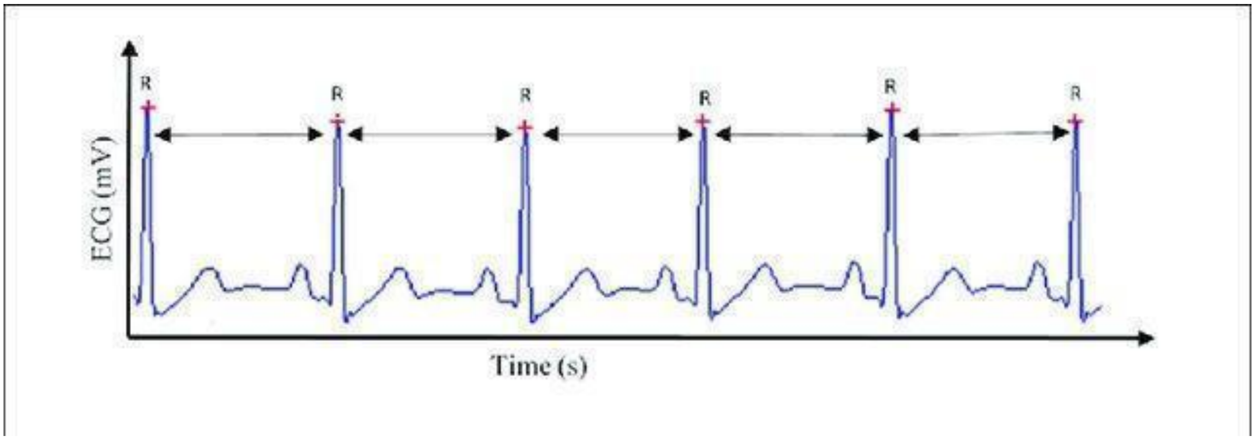

Figure 13: Differences in RR intervals forms heart rate variability [69].

As proven in many previous aero-medical studies, there is a direct correlation between amount and intensity of workload enforced to a pilot and the value of the HRV [13,14,15,19,66]. Rather than a physical load, airline pilots have more tendency to experience Mental Workload (MWL) due to the job's nature which obliges them to multi-task during every phase of flight. A good airline pilot is expected to aviate, navigate, communicate, and manage a diverse range of situations through a flight while sitting on a chair most of the duration. Which means that physiological changes in the subject's body mostly comes from the effects of adaptation to a situation or to a stressor rather than a result of a physical load. Because of this reason, HRV analysis can be used to define the amount of stress and fatigue that a pilot is facing, as well as it enables us to determine the length of the time a subject was exposed to a stressor or left in fatigued condition.

3.1.1 Effects of hormonal and neurological regulation

Changes in the time between two heart pulses, which is called as HRV, has a strong relationship with MWL and is caused by hormonal and neurological actions triggered by a stressor [70].There are two factors that determine HRV according to what subject experiences: hormonal changes and the response of Autonomic Nervous System (ANS) [71].

Hormonal control of HR is done with release of adrenaline and norepinephrine hormones, which increase the frequency of the heartbeat, and acetylcholine that decreases it [71]. Glucagon and insulin increases strength of the muscle contraction of the heart and speeds up the HR, while progesterone reduces it [71]. HR is also affected by the concentration of potassium and calcium ions in blood, body temperature, and atmospheric altitude or so-called density and pressure altitudes in aviation terminology [71]. Thyroxine hormone, which is produced by thyroid gland, affects the heart's sensitivity to catecholamine [71]. Increase in catecholamine concentration on blood was proven to be related to the increase in HR, and therefore, reduction of HRV, which indicates a presence of a stressor [71].

However, measuring the effects of hormonal changes due to stress on HRV would be too complicated to measure on pilots during simulated flying conditions, because this method would require to take samples of the subject's blood and test them for concentration of above mentioned hormones which would obviously disturb the flight tasks. Therefore, for our advantage, during our measurements we were interested in detecting the effects of neurological actions which are easily detectable by monitoring HR by ECG. Besides, measuring pilot fatigue in terms of hormonal changes in a subject's body does not seem a reliable and preferred approach in the aviation medicine literature.

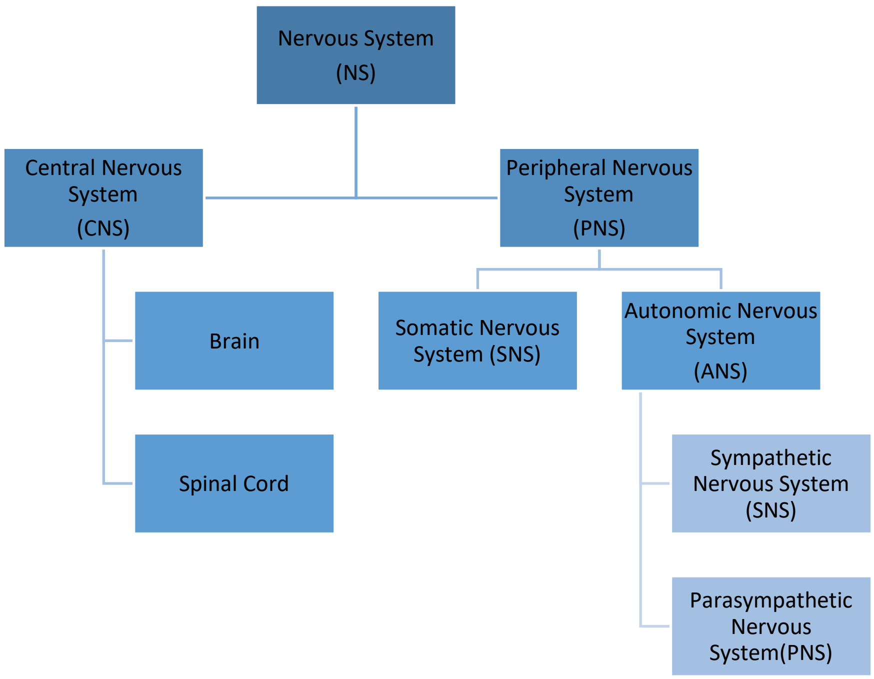

Figure 14: Structural division of the Nervous System [72].

The neuro-vegetative system works autonomously. It is made up of two subsystems with very differentiated actions: the Parasympathetic Nervous System (PNS) and the Sympathetic Nervous System (SNS). The PNS is generally sedative, directs homeostasis, activates the restoration of energy reserves in the body as well as cell reconstruction. It lowers the HR by the action of the vagus nerve on the heart. It is related to ventilation and the frequency of breathing. The SNS is generally stimulating and activating, directs the catabolism and activates the degradation of energy substrates to produce energy. It increases the HR as well as the force of contraction, myocardial. It helps to regulate blood pressure and vascular resistance [71].

Outcomes of activation of these two systems determine HRV according to events a subject experience. The SNS stimulates the body's fight-or-flight response. Meaning during a stressful situation in which immediate action is required, it is responsible for accelerating the HR, decreasing the HRV, contracting blood vessels, increasing blood pressure, and instructing hormonal glands to produce sweat [73]. On the other hand, the PNS does the opposite during the periods of rest, where the subject is not obliged to respond to any threat that disturbs his/her mental or physical state, it decreases the HR, therefore, increasing the HRV [73].

ANS controls automatic bodily functions and is associated with respiration, cardiac frequency, digestion and the hormonal system.PNS and SNS in this context provide a response to stress when a triggering action or relaxing situations are activated. By analyzing HR data of a subject who has been exposed to periods of change and a rest, the presence and duration of stress can be scientifically demonstrated [14,19,66].

The studies have shown a relation between PNS and SNS activity of ANS so called “sympathovagal balance” and components of HRV [13,14,15,19]. It can be said that HRV consists of two different spectral components, a component that lies in a low frequency (LF) band and the one that lies in a high frequency (HF) band. The LF component of HRV reflects sympathetic activity, whereas, the component that lies on the HF band represents vagal activity. This will be further discussed when the HRV analysis methods will be explained in the following chapter.

3.1.1.1 Cardiac activity during rest

Stress condition of an organism is particularly evident when it comes to rest periods since the average HR and respiratory rate becomes lower [12]. The average HR value lies anywhere between 61 to 72 beats per minute [74]. These values are even lower for young and healthy fit subjects who practice sport because of the exercises' ability to strengthen the heart tissue, allowing the heart to pump more blood with each stroke. An average healthy subject's HR is 50 beats per minute, while of the subjects who practice endurance training are 40 beats per minute [74]. This is accomplished by the repeated loading on the heart during endurance training which causes reduction in the resting heartbeat value with the constant activation of the PNS, which in return suppresses cardiac activity.

Children's and adolescent's heartbeat at rest is 10 beats higher per minute than adults, and this fact is also true for women because of having less leaner and smaller heart muscle [74]. The ideal resting heart rate is below 75 beats per minute since people with these values generally live longer. If the HR of a subject increases by about 10% then the normal, it may be caused by mainly stress, illness or insufficient recovery after a training [74].

3.1.1.2 Cardiac activity during workload and fatigue

When it comes to physical workload, highly trained individuals respond to a certain amount of workload with lower values than the ones with lower fitness level [75,76,77]. The fitness level of the subject can be judged by the variations in HR. In the pre-exercise state, the HR values increase by 20 to 40 beats / min, which is activated by nervous and hormonal stimulations due to adrenaline rush of the SNS [76]. The organism thus prepares for the incoming load and initiates transition from relatively low HRs to higher ones.

Important differences can be observed in the records between the subjects who are used to stress and those adapted only to the lower load level. The subjects who practice sports often exhibit a lower HR, lower respiratory rate frequency and the opposite is true for beginners: increased HR, also the level of catecholamines, consequently reduced self-confidence and accuracy [76]. From all these facts, we can conclude that a better physical condition increases the effect of PNS in reducing HR and improving emotional control. Thus, a fit subject generally has a lower HR and even faster after the stressor is removed from the environment.

When it comes to mental workload, above stated facts are confirmed by the researches focused specifically on pilots when the inexperienced pilots had a higher HR than the experienced captains during the same applied MWL and it was also proven that HRV is a significant indicator of the changes in workload during a flight [78].These changes can be caused by different flight situations (a flight over a high terrain, adverse meteorological conditions, sick or aggressive passenger on board) which are often accompanied by a feeling of distress and urgency. During previous studies, HRV is also proven to be sensitive to critical flight phases such as take-off, landing and instrument flight which is more demanding to a pilot than flying a visual flight [12,14,61]. High frequency components of HRV reduces during the approach and landing phases of flights, and similarly these components return to their initial baseline values when the flying task is ceased [14].

During a study in two different cockpit types (an analog cockpit and a glass cockpit) it was proven that stress condition that is caused by transferring 10 pilots from analog to glass cockpit has affected their HRV values which can be used to define the actual level of stress on pilots when they are forced to fly according to an unfamiliar cockpit avionics [12].

The measurement of the HRV makes it possible to specify the type of fatigue felt by an individual. For moderate complaints expressed, the LF / HF ratio during rest does not differ significantly, however, in cases of larger complaints of fatigue, there is a significant link between the modification of HRV, and the symptoms observed [78].This association is therefore not linked to the amount of work, but to the symptoms perceived by the patient. One could assume that exhaustion is linked to a dysfunction of the ANS.

We can conclude that HRV is a significant indicator of ongoing changes in the human organism. It can respond to physical and mental stress and represents the adaptation of the body to physical and mental workload conditions. As we have seen from the conclusions of the studies indicated previously,this frequency is rather irregular and its regularity is influenced by factors such as respiration, environmental influences, gender, age, training and medication [79]. Additionally, a completely regular sinus rhythm trend in HR is a negative prognostic factor that can be an indicator of cardiovascular disease or chronic stress [79].

The most widely used methods are based on the recognition of and measurement of RR intervals, representing dynamic series of cardiac intervals. This series is called the cardiointervalogram (CIG) and subsequent variability analysis (HRV) of these records are based on different mathematical methods such as time domain, frequency domain, and non-linear methods.

3.2 Analysis of HRV

Variability analysis is a method of evaluating HR. This method originated in the early 60's in the Soviet Union under space research. It is a method of evaluating the state of regulatory mechanisms and physiological functions of the organism, especially neurohumoral regulation of the ANS.

HRV is the fluctuation in HR over a period of time between two consecutive beats, and essentially depends on the extrinsic regulation of the cardiac frequency. While the HR may be stable, the time between two cardiac beats can be very different and its informative value is important for a subject's fatigue analysis. A reduction in HRV over a period of time indicates a stressed condition while an increase in HRV demonstrates removal of the stressor and condition of rest or comfort [13,14,15].

HRV reflects the heart's ability to adapt to a change, to detect and respond quickly to unpredictable stimuli. HRV is considered as a signal that reflects the activity of the ANS, and its analysis constitutes a non-invasive, reproducible and useful method of physiological investigation for assessing the state of the heart and the neuro-vegetative system responsible for regulating heart activity. When determining the HRV, HR fluctuations are considered recorded and analyzed over a period of time. An HRV measurement is carried out using a 24-hour ECG with a high sampling rate (1000 Hz) in time and frequency range, which represents a measure of the autonomic function of the heart and the state of the ANS.

Every person has an individual expression of the HRV, depending on age, gender, as well as psyche or medication [79,80].By finely tuned variations, the heart reacts individually to internal signals of the organism and external requirements. The HRV is strongest at rest and reduced during workload [13,14,15].

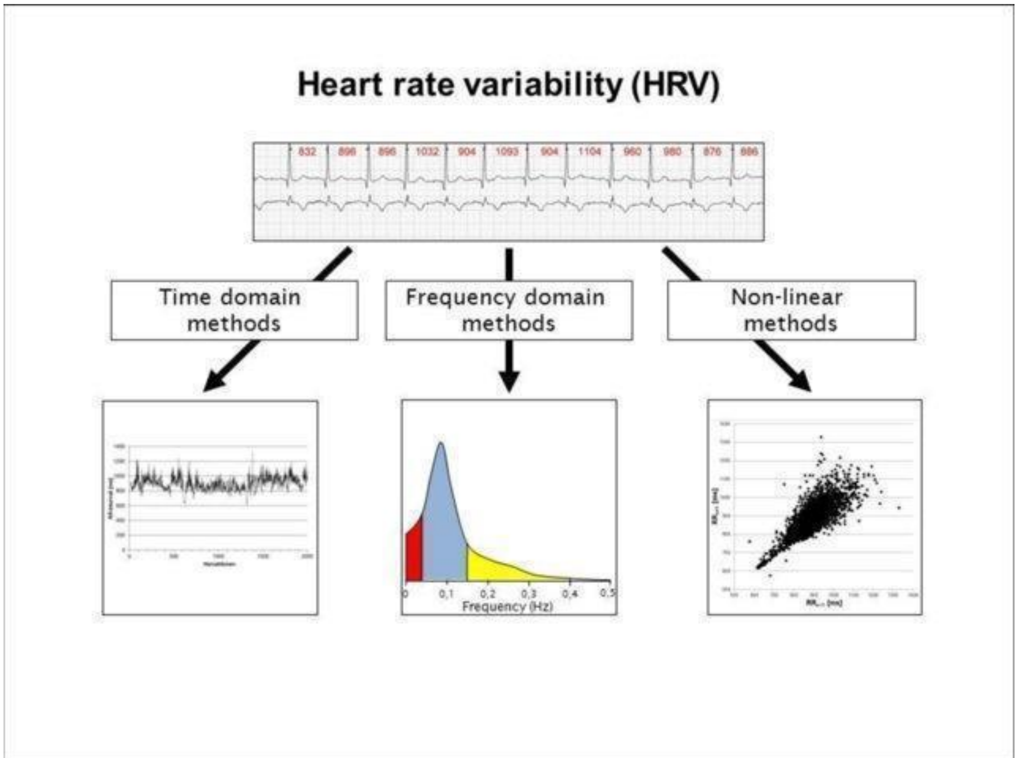

Figure 15: Types of HRV analysis used in fatigue studies [81].

HRV serves as a non-invasive diagnostic tool for the evaluation of autonomous function. Analysis of HRV is used not only in basic research but also in clinical medicine. It is used to assess the ANS of the heart and the balance between its two basic branches: sympathetic and parasympathetic systems. The autonomic activity of the sympathetic and parasympathetic affects the sinoatrial node and thus modulates the HR interval, which is known in an ECG signal as RR interval.

When performing an analysis of HRV, there are several mathematical methods to quantify the activities of ANS. Although each of them generates different clues, we will retain that they are all based on the same principle which consists of studying the evolution of the time differences between each RR interval. In other words, all the mathematical formulas for analyzing the HRV are based on a number sequence that represents the deviation time of all recorded RR intervals, usually expressed in milliseconds.

There are mainly 3 methods to analyse HRV. Time domain, frequency domain, and non-linear methods. All these signal processing techniques have only one goal: assessing the activity of the ANS in order to better understand certain pathologies or certain processes of adaptation to stress.

3.2.1 Time-domain analysis

HRV analysis can be performed and evaluated by a number of methods, perhaps the time-domain metrics are the simplest to accomplish this in the time frame. HRV can be made by measuring the times between the normal RR intervals and their standard deviations on the ECG. In these methods, the HR at any given time or intervals between successive normal complexes are determined. Each QRS complex is detected and then instantaneous HRV is decided.

The values obtained from RR intervals are displayed as a function of time on a graph so-called histogram. Histogram analysis makes the basis of all studies regarding HRV measurements. The indices of time-domain analysis are obtained with 2 different approaches: Statistical and geometric methods.

3.2.1.1 Statistical methods

Based on a series of instantaneous NN (Normal to normal) intervals recorded over a long period of time, usually 24 hours, more complex indices such as statistical time indices can be calculated.

These parameters can be divided into two groups:

1. Obtained by processing direct measurements of instant heart rate or NN intervals.
2. Calculated based on the difference between the NN intervals. These indicators can be calculated for the entire time of observation or for any specific intervals during the recording period, allowing us to compare HRV in different vital moments, such as sleep, rest, etc.

From a graphical point of view, the time domain is represented by a curve which is created by using a double time scale where each of the RR intervals is projected to the both on the x-axis and the y-axis.

The first information from this domain is the length of the RR intervals and the minimum and maximum observed during the measurement. We sometimes find the ratio "maximum / minimum" or the delta "maximum - minimum" which can inform us about the stationarity of the measurement during registration [82]. However, these first indices are not necessarily representative of the total registration since they are based on a single value which can unfortunately be biased [82]. Conversely, the researchers focused on fatigue studies give much more credit to time indices which are based on statistical formulas integrating all the RR intervals of the registration (represented by the number N in the following formulas). Therefore, the mostly used time-domain analysis indices are as following:

a) The simplest of all the indices is the average RR duration also abbreviated as **AVRR**, expressed in milliseconds which is the average time between two successive R-R peaks of the QRS complexes in a sample of ECG data.

$$\underline{RR} = AVRR = \frac{\sum_{j=1}^{N} RR_j}{N} \quad [83]$$

Where RR_j is the duration of the j-th RR interval, N is the number of all the RR intervals and $\underline{RR}$ is the average duration of all the RR intervals.

b) In any statistical analysis, it is essential to address the concept of standard deviation. The most convenient variable to calculate is the standard deviation of Normal to Normal intervals known as **SDNN**: the square root of the NN spread .Since the value under the root is mathematically equivalent to the total power in spectral analysis, SDNN reflects all cyclic components responsible for variability during the recording period [82]. In the literature, we regularly find this variable expressed in milliseconds and it is calculated with the following formula:

$$SDNN = \sqrt{\frac{1}{N-1}\sum_{j=1}^{N} (RR_j - \underline{RR})^2} \quad [83]$$

where RR_j is the duration of the j-th RR interval, N is the number of all the RR intervals and $\underline{RR}$ is the average duration of all the RR intervals.

The SDNN provides us with information on the distribution of values around the central (mean) value. This dispersion can be compared with the mean average using a coefficient of variation (relative standard deviation) calculation to consider the homogeneity of the RR intervals. From a physiological point of view, the SDNN index reflects the overall variability [82, 83]. This is the main indicator of the effects of ANS activity reflecting on HRV values.

In many studies, SDNN is calculated over the entire 24-hour period and thus includes short-term high-frequency changes and very low frequency components that occurred within a 24-hour measuring period. When the recording period is shortened, SDNN evaluates all shorter heart cycles. It should be noted that the magnitude of variability increases with increasing length of the studied record [80]. For an arbitrary ECG, SDNN is not the best statistical quantitative indicator due to its dependence on the length of the recording period.Therefore, the duration of the records on which the SDNN is supposed to be calculated should be standardized and ideally duration of the measurements should be 5 minute or 24 hour [80]. Because of this reason, our analysis is based on the values from 24-hour ECG measurements.

The most commonly used indicators determined from interval differences include RMSSD - the square root of the mean squares of the difference between adjacent NN intervals, NN50 - the number of cases in which the difference between consecutive NN duration exceeds 50 ms. , pNN50 – proportion of the intervals between adjacent NN in excess of

50 ms. to the total number of NN intervals in the record. All these indicators are highly correlated with high-frequency fluctuations in the structure of HRV [80,82,83].

c) The **PNN50** (Percentage of Normal to Normal Intervals) is obtained by making the ratio between the number of RR intervals that vary by more than 50 ms (in absolute value) with the previous interval and the total number of RR intervals of the record (N). Expressed as a percentage, this index is mainly modulated by the parasympathetic activity of our ANS, therefore indicating a condition of comfort or absence of a stressor exerted on a subject.

$$pNN50 = \frac{(|RR_j - RR_{j-1}|) > 50\ ms}{N-1} \times 100 \quad [80]$$

where RR_j is the duration of the j-th RR interval, N is the number of all the RR intervals.

d) Finally, we must also mention the **RMSSD** (Root Mean Square of Successive Differences of RR intervals) which is the most widely used index in the literature. Expressed in milliseconds, it is calculated by making the square root of the mean of the squared differences of successive RR intervals and it also represents the parasympathetic activity of our ANS, therefore again indicating a condition of comfort or absence of a stressor exerted on a subject [83].

$$RMSSD = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1} (RR_{i+1} - RR_i)^2} \quad [83]$$

$$rr_i = \frac{2(RR_i - RR_{i-1})}{RR_i + RR_{i-1}} \quad [83]$$

Where $RR_{i+1}, (i = 2, \ldots, N)$, relatively determines the RR interval. And, where RR_i is the duration of the i-th RR interval and N is the number of all the RR intervals.

Overall, a connection can be made between the different indices of the time-domain method and, in general, the decrease in one of these indices is often associated with an unfavorable diagnosis (fatigue, cardiovascular risks, overtraining, etc.)[80,82,83].

3.2.1.2 Geometric methods

The sequence of NN intervals can also be converted to a geometric structure such as density distribution of duration of NN intervals,the density distribution of the difference between adjacent NN intervals, Lorentzian distribution, etc. Then a simple formula is applied, which allows to evaluate variability based on geometric or graphic model properties. When working with geometric methods there are three accepted approaches:

1. Main dimensions of the geometric model (e.g. width distribution histograms at a certain level) are converted into measurements HRV,

2. In a certain mathematical way (approximation of the histogram distribution of a triangle or differential histogram exponential curve) the geometric model is interpolated and further analyzed by coefficients describing this mathematical form,

3. Geometric form classified, several categories of geometric shapes are distinguished, representing different classes of HRV (elliptic, linear, triangular Lorentz curve).

   Most geometric methods require the sequence of NN intervals that was measured or converted to be in discrete scale which allows us to get reliable histograms. Most commonly used sampling rate 8 ms (1/128 seconds), which corresponds to the possibilities of commercially available equipment [82].

a) **The HRV Triangular Index** is defined as the integral of the distribution density of the total NN intervals, divided to the maximum distribution density. While using a discrete scale of NN intervals, its value may depend on sampling rates. It is based on a histogram where 128Hz is applied between RR intervals [82].

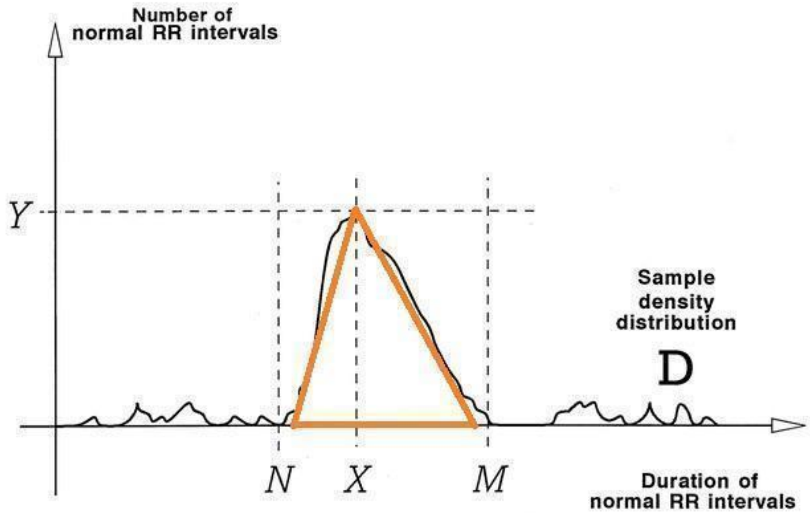

Figure 16: Calculation of the triangular index and TINN are shown [84].

Both of these measurements express the total heart rate variability measured over 24 hours and are more dependent on low-frequency than on high-frequency components [84]. NN integral length is defined as X, therefore, Y=D(X) example density distribution is the maximum value of D. HRV triangular index is determined by the highest X value which has the frequency Y, and it can be expressed by the following formula:

$$HRV\ triangular\ index = \frac{N}{Y} \quad [84]$$

where N is the total number of NN intervals. The triangular index is the value which is obtained by dividing the area integral of D to maximum Y. Therefore, we can say that the HRV Triangular Index is Total number of all RR intervals (N) divided by the height of the histogram of all RR intervals (Y).

b) **TINN** (Baseline Width of the RR Interval Histogram) is the baseline with length of triangular interpolation of the square difference of the highest point of the RR interval histogram that was measured according to 1 / 128s sampling rate [84].

$$TINN = M - N \qquad [84]$$

Where M and N are the edge points of the combination of triangular functions of t<N , t>M for T(t)=0 as shown on the figure 16. For obtaining TINN value, the triangular interpolation of RR intervals is used, where M and N is the baseline width of the triangular interpolation.

The main advantage of geometric methods is their relative insensitivity to the analytical quality of a series of RR intervals [80]. The biggest disadvantage is the need for an acceptable amount of NN- intervals for constructing a geometric model. In practice, for application of geometric methods, we need to use records not shorter than 20 minutes but preferably 24 hours as we did in our measurements [80]. Modern geometric methods are not suitable for evaluating rapid changes in variability,however, they are more useful in determining the long term impacts [80].

Parameter	Unit	Description
	Statistical Parameters	
SDNN	*ms*	Standard deviation of NN intervals
SDRR	*ms*	Standard deviation of RR intervals
SDANN	*ms*	Standard deviation of the average NN intervals for each 5 min. segment of a 24h. HRV recording
SDNN index (SDNNI)	*ms*	Mean of the standard deviations of all the NN intervals for each 5 min. segment of a 24h. HRV recording
pNN50	%	Percentage of successive RR intervals that differ by more than 50 *ms*
HR Max – HR Min	*bpm*	Average difference between the highest and the lowest HR during each respiratory cycle
RMSSD	*ms*	Root mean square of successive RR interval differences
	Geometric Parameters	
HRV Triangular Index	N/A	Integral of the density of the RR interval histogram divided by its height
TINN	*ms*	Baseline width of the RR interval histogram

Table 5: Time-domain indices of HRV analysis [80].

3.2.2 The frequency-domain analysis

Basic information on power distribution as a function of time is provided by power spectral density analysis (PSD). Using suitable mathematical algorithms can only be obtained by estimation of the actual PSD signal, independent of the method used. Methods for computation of PSD can be classified into parametric and nonparametric methods. In most cases both groups of methods give comparable results [80].

Advantages of the nonparametric methods are:

- The simplicity of the algorithm used (Fast Fourier transform - FFT)
- Quick computation

while the advantages of parametric methods are:

- Smoother spectral components, distinguishable independency of pre-selected frequency band,
- Simple processing of the received spectrum with automatic calculation of low-frequency and high-frequency spectrum components and simple identification of the fundamental frequency of each component,
- An accurate estimate of the power spectral density even for a small number of samples where the signal is assumed to be stationary.

In the spectrum for shorter measurement periods, power is divided into three main components - very low frequency (VLF), low frequency (LF) and high frequency (HF). Additionally, for 24-hour recordings an ultra-low frequency (ULF) component is distinguished [80]. Power distribution and central LF and HF frequencies are not fixed, but may vary depending on changes in autonomous HR modulation as can be seen in the figure 17.

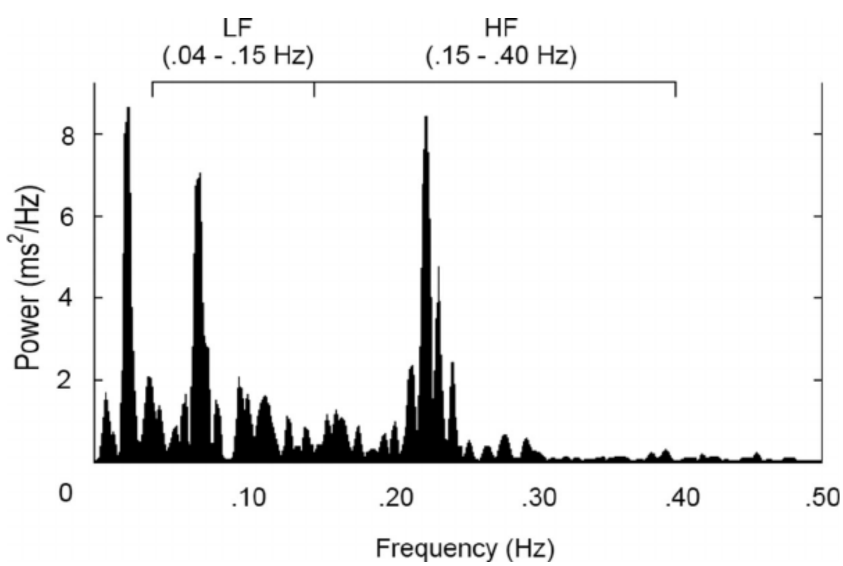

Figure 17: An example of a heart rate variability power spectrum [85].

- **The VLF (Very Low Frequency)** component of PSD has a frequency range of 0.01 - 0.04 Hz. In general, the main part of this component is attributed nonparametrically to a component that does not have coherent properties and is affected by baseline properties.This is a mixed measure of baroreceptor reflex activity because it affects blood pressure along with parasympathetic and sympathetic activities [86]. Physiologically, the VLF reflects the mechanisms of long-term regulation such as thermoregulation or hormonal regulation. However, because of its difficulty in interpretation, the VLF component is rarely considered within HRV analyzes [80].

- **The LF (Low Frequency)** component of PSD has a frequency range of 0.04 - 0.15 Hz. It is an indicator of sympathetic and parasympathetic activity. It is also stated that it represents the result of baroreflex activities [86]. With an increase in sympathetic activity, there will be an increase in LF performance [82].

- **The HF (High Frequency)** component of PSD has a frequency range of 0.15 - 0.4 Hz. The HF is strongly connected with cardiac activity of the vagus. The respiratory variation observed during the cardiac period is directly proportional to the parasympathetic control of the heart rate and its modulation forms the theoretical center in most HRV analyzes [82]. In order to be able to measure parasympathetic activity using HF, it is important so that the respiratory rate is high and lies in the HF frequency range [82]. If this condition is not met, HF provides only a measurement of noise[82].

Measurements of VLF, LF and HF power components are usually given in absolute units of power, but LF and HF can also be measured in standard units (nu).The normalized values (LFnu, HFnu) are calculated from the original values of any of the two short-term frequency bands (LF or HF) divided by the total spectral power (LF + HF) [80].

Therefore, we can summarize that the basis of the frequency-domain HRV analysis is the evaluation of amplitudes of the HR at different rates. LF is affected by the SNS and PNS activities. Whereas, HF is affected only by the PNS. Sympathetic values are evaluated to determine the magnitude of the MWL inserted on a subject [13,14,15].

$$SNS_{(i)} = \frac{LF_{(i)}}{HF_{(i)}} \quad [80]$$

where LF is the low frequency amplitude of the spectrum of the RR interval and corresponds to the sympathetic activity, while HF is the high frequency amplitude of the spectrum of the RR interval and corresponds to the parasympathetic activity.Thus, an increase in CIS means an increase in mental stress [12,17,18,87].

Before describing the various indices of the frequency domain analysis, it seems important to illustrate what, from a mathematical and physical point of view, the frequency domain of a signal represents. Based on a theory enunciated by Joseph Fourier in 1807, the frequency domain is the representation of a periodic function as an infinite sum of trigonometric functions of multiple frequencies of a frequency fundamental [88]. In other words, any time signal, periodic or stationary, can be described using a function composed only of a sum of sinusoids of different frequencies and amplitudes such as:

$$f(x) = a_0 + \sum_{n=1}^{\infty} \left(a_n cos\ \frac{n\pi x}{L} + b_n sin\ \frac{n\pi x}{L} \right) \quad [88]$$

The transition from the time domain to the frequency domain of a signal takes place using a Fourier transform which has the formula:

$$f(v) = \int_{-\infty}^{+\infty} f(t)\, e^{-i2\pi vt}\, dt \quad [88]$$

More specifically, we usually represent a signal in the frequency domain using a graph representing the power spectral density (PSD) where the *x*- axis represents frequencies (in Hertz) and the *y*- axis represents amplitudes (power in $milliseconds^2$for HRV) of each of the frequencies composing the signal as in the figure 17. Using a Fourier transform, this same signal can be represented in the frequency domain via its power spectrum such as shown in the figure 18. In the same way as in the time domain, we can see that the signal is composed of a single sinusoid (a single spectral line).

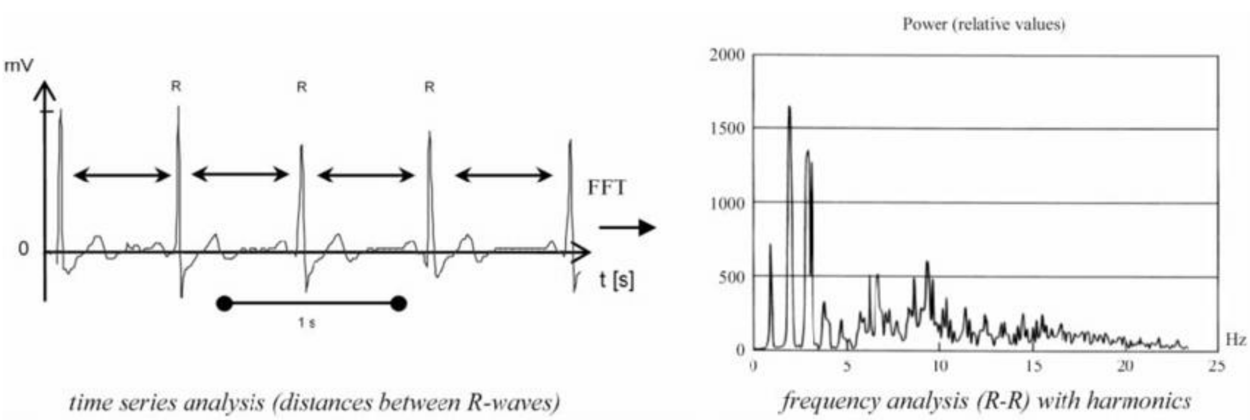

Figure 18: An example of a Fast Fourier Transform that is used to convert the RR intervals from time-domain analysis to frequency domain analysis [89].

As a conclusion, the frequency domain is just another method of representation of a stationary and periodic signal that we utilize in the time domain method. Nevertheless, it presents a number of advantages, the most important of which is to be able to dissociate several sinusoids of different frequencies which, in the temporal representation, remains obviously impossible to achieve.

The LF / HF ratio represents the sympathovagal balance of ANS. In fact, it allows us to immediately determine what is the dominant frequency band. It has been proven that stress exerted on pilot subjects increases sympathetic activity as can be seen in the LF component of HRV, which also increases the LF/HF ratio [12,13, 14,15,19]. Therefore, LF/HF ratio is often used in fatigue studies to describe sympathovagal balance. Therefore, even though there is no standard general rule to determine metal stress solely based on LF/HF ratio, it is a common way of determining a quantitative indicator of the activity of the ANS related to mental stress and to develop a score which can be used to evaluate MWL during tasks of varying complexity.

Finally, the last frequency- domain parameter is the **TP (Total Power)** of the spectrum. This index represents the area under the power spectral density curve. In other words, it is equal to the sum of three frequency bands VLF, LF and HF. Parseval's theorem shows that there is a conservation of energy between time and frequency domains which results in the equality of the variance and the total power of the signal [90]. More specifically, the frequency-domain parameter TP is mathematically equal to the time marker $SDNN^2$ but this equation cannot be verified in practice since it depends on the method of signal processing used [91]. However, there is a well known consensus in the literature that the TP index is strongly correlated with the SDNN index of the time-domain analysis of HRV[91,92].

In a previous study, HRV was also studied to argue if a pilot is confident and qualified enough to perform a particular flight maneuver. The results from HRV metrics (SDNN,RMSSD, LF/HF ratio) that were measured before and during a simulated flight in a Federal Aviation Administration (FAA) certified A320 simulator on 30 actively flying commercial airline pilots have proven that pilots were performing a specific given task with a higher accuracy when his/her response to a stressor was lower, as indicated by higher SDNN and RMSSD and lower LF/HF ratio [13].

To summarize, we can conclude that the most important parameters of the frequency-domain analysis and their meaning on ANS activity are:

Parameter	Unit	Description
ULF power	ms^2	Absolute power of the ultra-low-frequency band (≤0.003 Hz)
VLF power	ms^2	Absolute power of the very-low-frequency band (0.0033-0.04 Hz)
LF peak	Hz	Peak frequency of the low-frequency band (0.04-0.15 Hz)
LF power	ms^2	Absolute power of the low-frequency-band (0.04-0.15 Hz)
LF power	nu	Relative power of the low-frequency-band (0.04-0.15 Hz) in normal units
LF power	%	Relative power of the low-frequency-band (0.04-0.15 Hz)
HF peak	Hz	Peak frequency of the high-frequency band (0.15-0.4 Hz)

HF power	ms^2	Absolute power of the high-frequency band (0.15-0.4 Hz)
HF power	nu	Relative power of the high-frequency band (0.15-0.4 Hz) in normal units
HF power	%	Relative power of the high-frequency band (0.15-0.4 Hz)
LF/HF ratio	%	Ratio of LF-to-HF power

Table 6: Frequency-domain indices of HRV analysis [80].

3.2.3 The non-linear domain analysis

Several methods of analysis can be associated with the non-linear domain of the HRV which, by definition, reflects the fact that the output (effect) of a physical system is not proportional to its input (action) [82]. This method is used to determine HRV in a non-linear manner since not all the interactions between the SNS and PNS are linear.There are two indices that refer to the non-linear domain method of HRV analysis: **SD1** and **SD2**.

These two indices come from the diagram representation of the Poincaré graph (see Figure 19). In this graph, each coordinate point (x,y) is constructed by using two consecutive RR intervals such that: the duration of the current RR interval (RR_i) is shown on the x- axis , and the duration of the next RR interval (RR_{i+1}) is shown on the y axis. Each point in these plots serves to display duration of RR interval and duration of the following next RR interval. The line of the function x=y ($45°$angle) represents equal RR intervals. The points that are above the reference line (x=y) are longer RR intervals, while the points below it represent the shorter RR intervals.

As a rule of thumb, the subjects who experience rest or state of comfort have eclipse or comet shaped plots that disperse with longer beats while the subjects who are exposed to a stressor or are fatigued demonstrate “a torpedo” or “complex shaped” patterns [93]. In addition to that fact, mostly, if the Poincaré graph is compact it indicates a worse HRV state, meaning a presence of a stressor, while an extended and wide-spread plot represents a good HRV state, meaning an absence of a stressor [93].

As shown in the figure below, SD1 represents the standard deviation of the points along the axis which is perpendicular to the reference, and SD2 represents the standard deviation of the points along the axis of the reference line.

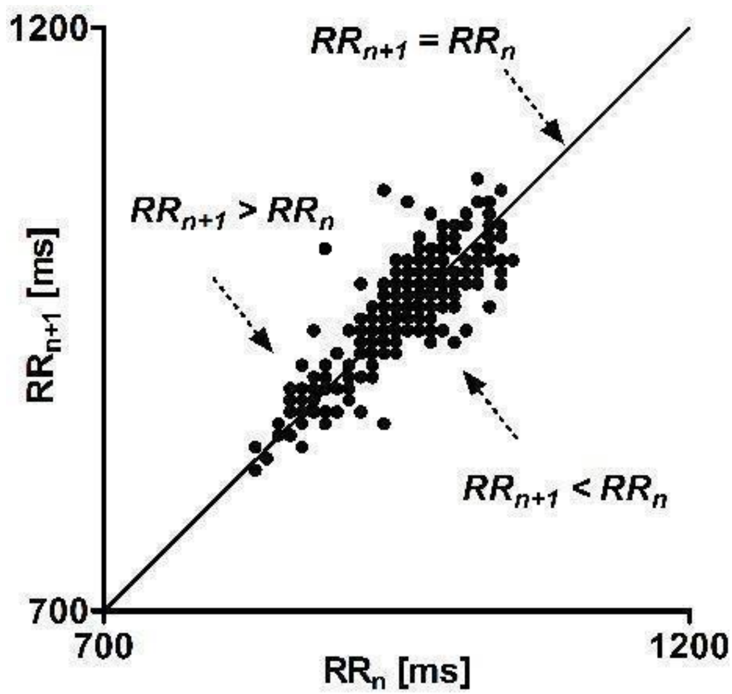

Figure 19: Representation of the Poincaré diagram of a recording of HRV where each point (x, y) is placed using two adjacent RR intervals (RR_n , RR_{n+1}) [94].

To summarize, the non-linear indices SD1 and SD2 are based on the calculation of standard deviations along the x=y axis and the perpendicular axis. From a mathematical point of view, SD1 and SD2 can also be calculated directly without necessarily going through the Poincaré representation using the two following equations [95]:

$$D_{i(min)} = \frac{RR_i - RR_{i+1}}{\sqrt{2}}$$

$$D_{i\ (max)} = \frac{RR_i \ + RR_{i+1} - 2\underline{\underline{RR}}}{\sqrt{2}} \qquad [95]$$

$$SD1 = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N-1} \quad D_{i(min)}^2}$$

Physiologically speaking, the SD1 index mainly represents the parasympathetic activity of a subject and is correlated with the RMSSD time index [95]. On the other hand, the SD2 marker rather reflects the overall activity of the subject and has a close relationship with the SDNN time index [95].

$$SD2 = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N-1} \quad D_{i(max)}^2}$$

$$SD1 = \frac{RMSSD}{\sqrt{2}}$$

$SD2 = \sqrt{\frac{2SDNN^2 - RMSSD^2}{2}}$; where SDNN and RMSSD are previously defined [95].

The fact that there are strong similarities between these two non-linear indices (SD1,SD2) and some indices of the time-domain method (RMSSD, SDNN) somewhat reduces their usefulness, however, this method provides us a significant visual graphical data through the representation of Poincaré plots. The Poincaré plot below displays HRV differences between non-overtrained and overtrained subjects which enables us to identify the state of fatigue in the case of overtrained subjects [96].

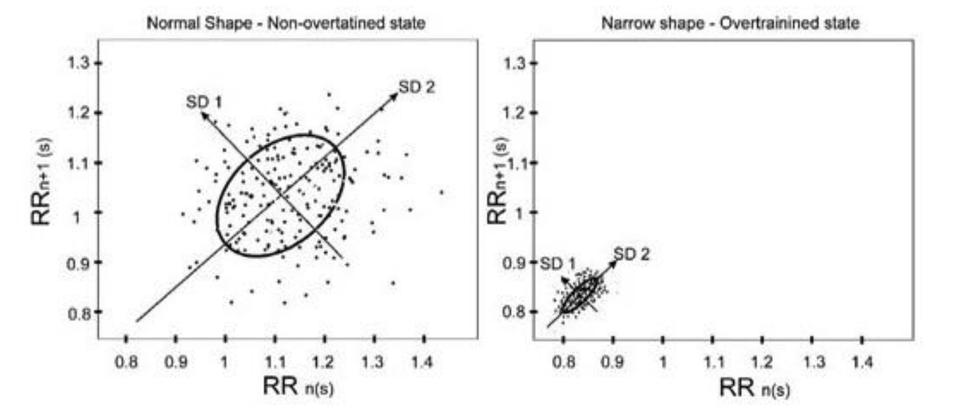

Figure 20: Poincaré representation of a HRV recording made on a subject normally trained (left figure) and a subject medically diagnosed as overtrained (right figure) [96].

Although the usage of Poincaré plot remains fairly controversial within the HRV-fatigue related literature, we retain that the majority of other indices in the nonlinear domain are based on the chaos theory. Thus, most of those algorithms are intended to indicate determinism of a signal by accounting for its complexity [80]. As an example, the dimension fractal, DFA function (detrended fluctuation analysis), approximate entropy (ApEn), or the correlation dimension (D2) are among the other indices of nonlinear methods.

However, from a practical point of view, most of these algorithms are not often used in analysis of HRV. Two causes can be cited to justify this reason: First of all, these analytical methods are difficult to understand and to put into practice. Secondly, their physiological interpretation regarding fatigue is not agreed within the scientific community which is not the case with SD1 and SD2 indices.Therefore, during the nonlinear analysis of our pilot subjects' ECG data, only SD1 and SD2 indices and their plot on Poincaré is used to determine their fatigue condition.

Parameter	Unit	Description
S	ms	Area of the ellipse which represents total HRV
SD1	ms	Poincare plot standard deviation perpendicular to the line of identity
SD2	ms	Poincare plot standard deviation along the line of identity
SD1/SD2	%	Ratio of SD1-to-SD2
ApEn	N/A	Approximate entropy, which measures the regularity and complexity of a time series
SampEn	N/A	Sample entropy, which measures the regularity and complexity of a time series
DFAα1	N/A	Detrended fluctuation analysis, which describes short-term fluctuations
DFAα2	N/A	Detrended fluctuation analysis, which describes long-term fluctuations
D2	N/A	Correlation dimension, which estimates the minimum number of variables required to construct a model of system dynamics

Table 7: Table 7: Non-linear domain indices of HRV analysis [80].

3.2.4 Time-frequency domain analysis and methodological plurality

Although this thesis work is not specifically dedicated to the different methods of HRV signal processing, we aim through this section to illustrate briefly and without necessarily going into detail the possibilities that are available to the researcher to move from time-domain representation to frequency-domain representation of the ECG signal. As mentioned previously, the best-known method is the Fourier transform (non-parametric) and the autoregressive modelling (parametric method), however, there are also other algorithms such as the wavelet transform, or the the Wigner-Ville method which is as well based on a different kind of analysis so called time-frequency domain analysis.

Time-frequency analysis is a technique that simultaneously includes and examines a signal in both time and frequency domains using various time-frequency representations. Instead of utilizing a 1-dimensional sign as a function, real or complex values and some transformations, time-frequency analysis works on two-dimensional signs [97]. Similar to the frequency-domain analysis, time-frequency domain analysis measures the parameters of VLF, LF and HF components.

The practical motivation for time-frequency analysis is that it assumes that the signs of classical Fourier analysis are infinite in time or periodic [97]. And, in practice, many characters are of short duration and change significantly over their course. The mathematical motivation of this analysis is that functions and transformation representations are set as a two-dimensional object which is closely linked and not separate from each other [97]. Therefore, these parameters can be better understood when they work together.

Time-frequency HRV analysis measures the frequency components of VLF, LF and HF, as in the same as frequency-domain analysis. There are several approaches in order to convert time-domain function distribution to a formula which creates different time-frequency distributions:

- Short time Fourier transform (STFT) [97].
- Wavelet transform (relatively newer approach allows to analyze and compress many timestamps at once) [99].
- Auto-regressive modelling (ARM) [98].

Each of the previously cited methods can be found in the fatigue studies, nevertheless, we can observe that there is unfortunately no methodological consensus on the most appropriate algorithms to study HRV [82,86,100]. In other words, to our knowledge, there is no literature review that offers a clear, precise and completely objective opinion on the matter and, generally, most of them are content to present the advantages and disadvantages of several methods by concluding that each provides similar and comparable results [98,101]. It is important to emphasize that this methodological plurality is also found within an autoregressive analysis (with the choice of order and model selected) or of a wavelet transform (with the choice of the mother wave shape, the factor scale and translation parameter) [101]. In other words, the researcher is faced with many methodological choices, whatever the signal processing algorithm retained. From a practical point of view, the absence of a clear and precise consensus leads to many controversies and makes any rational comparison of similar studies difficult. During our HRV analysis, we will use the Fourier transformation which remains the most popular method that is used in the fatigue studies.

As a conclusion , we will retain that several markers can be calculated from a RR interval recording (see Table 8). Grouped within 3 domains (time, non-linear and frequency), some of these indices reflect the global activity of the autonomous system while others allow to separate the activity of the branches sympathetic and parasympathetic. Although each parameter has a certain interest, it is important to emphasize that the fact of presenting the evolution of all of these indices within the same study can complicate the physiological interpretation of the results that follow.

Analysis Type	Parameter	Indication
Time-domain	*AVRR (HR) (bpm)*	Average cardiac frequency
	SDNN (ms)	General variability
	RMSSD (ms)	Short-term variability: Parasympathetic activity
	pNN50 (%)	Short-term variability : Parasympathetic activity
Non-linear	*SD1 (ms)*	Short-term variability : Parasympathetic activity
	SD2 (ms)	General variability
Frequency-domain	*VLF (ms²) [0-0.04] Hz*	Sympathetic and Parasympathetic activity
	LF (ms²) [0.04-0.15] Hz	Sympathetic and Parasympathetic activity
	HF (ms²) [0.15-0.4] Hz	Parasympathetic activity
	TP (ms²) [0-0.4] Hz	General variability
	LF/HF	Sympathovagal balance

Table 8: Summary of the main indices of HRV analysis [80].

Overall, we can summarize the effect of neurological systems on HRV with the following scheme:

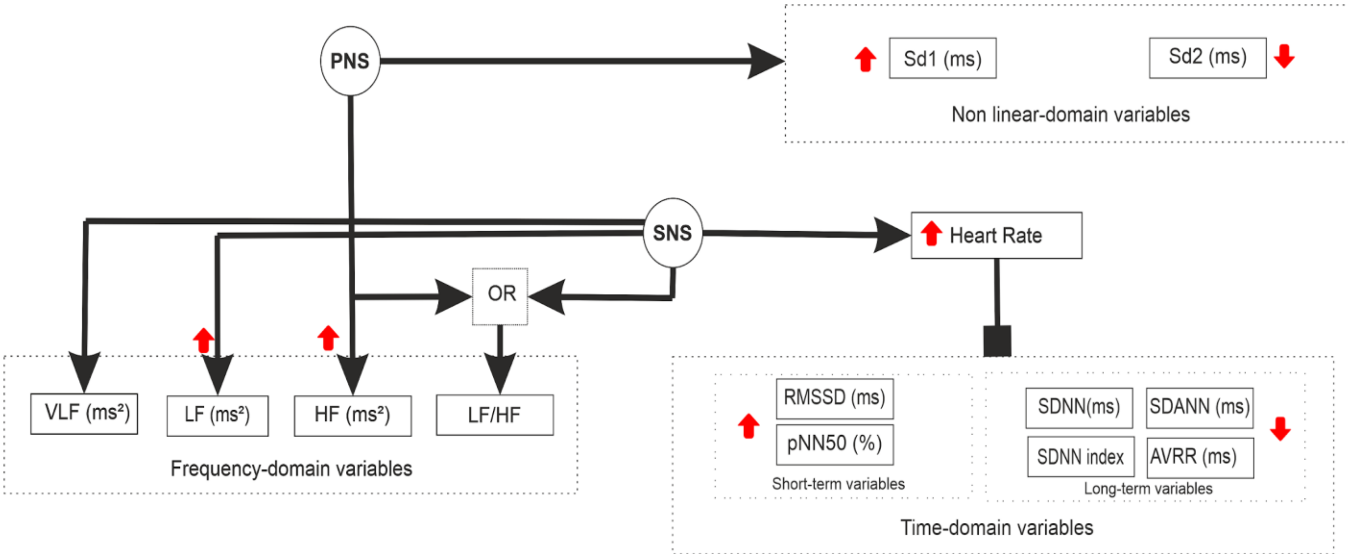

Figure 21: HRV parameters characterizing the ANS. Arrows indicate a decrease (↓) or increase (↑) in indicator activity.

Basically, we can say that with an increase in HR, we observe a direct relationship and an increment on the frequency-domain variables, an inverse relationship and a decrement in long-term time-domain variables, a direct relationship and an increment in short-term time domain variables. Also, SD1 has a direct relationship with the heart rate fluctuations, and SD2 has an inverse relationship with the changes in heart rate.

3.2.5 The problem with the diversity of HRV parameters

As indicated in the table 8 and the figure 21 above, each of the HRV indices reflect the activity of the sympathetic and parasympathetic branches of our autonomic nervous system. Although each marker has different raw values, it appears that strong similarities exist between several of them as we have seen in the previous chapters.In fact, it has been shown that there are, in terms of variation, significant correlations between RMSSD and SDNN as well as between the SDNN and TP indices. Additionally, we have seen a correlation between the RMSSD and SD1 indices as well as between the SDNN and SD2 indices. In other words, presenting the RMSSD and the SD1 results on a research article is simply to publish the same information twice.Thus, to eliminate the redundancy, we will apply linear regression analysis in the following chapters to find out the best indices representing HRV results.

Similarly, it is very common to find in certain works the results of frequency indices expressed in raw values (LF and HF), in standardized unit (LFnu= 100 x LF / (LF + HF) and HFnu = 100 x HF / (LF + HF)) as well as in the LF / HF ratio format [16]. We can clearly see that the last 3 indices represent the same value of the first two pieces of information only in a different mathematical format. Therefore, it would be interesting to ask why many researchers insist on publishing the results of each HRV marker at risk of presenting the same information several times and making the content confusing to the reader who will quickly overwhelmed by all these results without necessarily being able to isolate the causes and to attribute the effects on each of the indices studied.

In order to illustrate our point: even though there is currently no norm that would determine the extent of mental stress solely based on LF/HF ratio, evaluation of stress using only this HRV parameter is utilized in many pilot fatigue related studies [12,17,18]. Whereas, in some others, the three of the most common SDNN,RMSSD,LF/HF ratio HRV indices are considered to assess pilot fatigue[13]. In a different study that combines objective and subjective measurements of pilot fatigue by using heart rate variability and NASA-Task Load Index, LF/HF, SD1, SDNN indices are discussed during workload analysis [19]. There are also studies done which claim to show mental workload and fatigue experienced by pilots only by analyzing the amplitudes of maximum heart rate and minimum heart rate results (HRmax-HRmin) [14]. While some other studies found it necessary to analyze the values of many HRV parameters all together for the analysis such as: RR, SDNN, SD1, SD2, LF+HF, LF/HF, LFnu, HFnu [15]. Although each parameter has a certain interest, it is important to emphasize that the fact of presenting the evolution of all of these indices within the same study can complicate the physiological interpretation of the results that follow.

It seems that proposing a list of the most significant parameters to the scientific community would tremendously help to strengthen the hypothesis initially formulated by demonstrating the existence of a non-causal link only with the overall HRV but also with a multitude of underlying indices. Conclusively, the fact that focusing on the analysis of a single index makes it possible to better target the underlying mechanisms that modulate it. Despite the relative evidence of the robustness of some parameters of HRV, there is still no consensus on the most accurate index for fatigue studies. Therefore, our purpose in this work is to come up with the global set of indices that provides the most accurate results.

3.3 Factors affecting HRV analysis

Each of the previously described indices are under the permanent influence of many parameters that can significantly modify the result of a HRV analysis. Thus, it is necessary to take into account or even control these variables according to the methodological framework of each study. In view of the range of parameters that can influence the results, we retain only those which in our opinion seem relevant in the context of a use of the HRV analysis on pilots during simulated flight conditions.

3.3.1 Time of measurement

Nervous control of the cardiovascular system follows a circadian rhythm that results in large differences between the diurnal and nocturnal phases. From a point of view of the HRV, the results of an analysis can largely fluctuate according to the time of the day in which the recording is made. More specifically, the autonomic activity exhibits a strong sympathetic dominance during the day for an individual who is usually awake during the daytime while, during the night, we can observe an increase in parasympathetic activity which remains elevated for the first few hours after waking up [102].

This influence of the nycthemeral rhythm on the activity of the ANS appears very important since several studies show that it persists despite sleep deprivation. In a study on 50 subjects without an obvious heart disease, it was found that night time HR and total HRV was lower, additionally, VLF,LF and HF components of the spectral density were higher. Which indicates the presence of parasympathetic activity. The RMSSD decreased significantly during the night phase (value recorded at 2 a.m.), during the diurnal phase going back to values similar to the previous day[102].

We will retain that, for subjects who maintain a stable living environment (ie. regular alternation between wakefulness and sleep), all parameters of cardiac variability reach their acrophases around 2-3 a.m. and their bathyphases around 2 p.m. except for the LF / HF ratio which exhibits inverse kinematics [102]. Such variation encourages us to take the circadian rhythm into account when analyzing HRV since the value of the different parameters will also depend on when the registration is done.

3.3.2 Position of subject

On earth there is a permanent interaction between our body and the ground called gravity. This gravitational force interacts differently with our body and the position we adopt (lying, sitting, standing). The ANS is then solicited, via baroreceptors, to regulate our blood pressure and adapt our cardiac rhythm as a function of postural stress [103].Given the close relationship between the ANS and HRV, it seems important to consider the position of our subjects during measurements.

Many studies have focused on the influence of posture to HRV analysis and it turns out that the comparison between lying and standing positions is the most frequently discussed in the literature [103,104,105]. We can assume that each variable of HRV is significantly affected by the subject's position. Thus, the time indices such as SDNN, RMSSD or even pNN50 represent lower values in the standing position compared to the lying position [103]. From a frequency point of view, the same condition applies for the TP and the HF component, however, we encounter with unlike activity on LF components, which presents higher values in a standing position rather than in position lying down [103].

This phenomena could be explained as: When standing, blood from the central venous system has a tendency to move towards the lower limbs, thus causing an increased sympathetic vasomotor activity.This happens in order to preserve the blood pressure and to prevent the individual from falling into vagal syncope. This increase in sympathetic activity is also triggered by the need to activate muscle posture that helps maintain balance. Conversely, we observe a greater parasympathetic activity when lying down [103,104,105]. This dominance can in part be explained by the appearance of strong vagal stimulation that allows respiratory synchronization (respiratory sinus arrhythmia).

We can also point out that some authors study the results of a tilt test [106]. This test involves taking the subject from the lying position (0°) to standing position (90°) with a tilting table or when standing up quickly. This sudden change in posture is a simple and effective way to produce acute effects on the autonomic activity by stressing the limb that causes activation of sympathetic branches during the standing position. This change of posture causes blood to flow from the upper body to towards the limb and therefore a sudden drop in blood pressure is observed [106]. In the subjects, the stimulation of cardiac mechanoreceptors and arterial baroreceptors proportionally leads to a physiological response resulting in an increased HR [106].

We will retain that the posture of the subject during a recording of HRV must necessarily be included in the list of controlled variables since any change in posture leads to significant changes in terms of indices. Therefore, we paid an additional attention that our pilot subjects maintained their posture as much as possible while they had to reach out for flying charts and cockpit switches.

3.3.3 Respiration rate

There is a permanent interaction between cardiac and respiratory functions. Inspiration temporarily inhibits the influence of the PNS and produces an acceleration of the HR and, conversely , expiration stimulates the PNS and induces a slowing down of the HR [107]. The origin of these oscillations produced by respiration, so-called respiratory sinus arrhythmia, may be associated with several factors. Firstly, it is due to the direct influence of respiratory medullary neurons on the cardiomotor muscles [108]. Then, the stimulation of baroreflex activity plays a role due to the increase in blood pressure during the inspiration phase, which leads to these variations in the activity of the ANS [108] . Finally, the cardiopulmonary baroreceptors or stretch receptors of the lung may also participate in this cardiorespiratory interaction [108].

From a functional point of view, respiratory sinus arrhythmia plays an active physiological role since it allows to promote gas exchange during the inspiration phase when the air entering the lungs presents a high oxygen content. Conversely, it makes it possible to slow down the gas exchanges during the expiration phase where the residual air in the lungs has a high in carbon dioxide.

According to the studies, respiratory sinus arrhythmia seems more or less pronounced depending on different parameters such as the frequency of spontaneous breathing, fitness level or psychological stress level (ie. anxiety) [108]. When observing a HRV recording of a subject with a strong respiratory sinus arrhythmia, we may see a sine wave in every period which coincides with a breathing cycle of the subject. From a frequency point of view, this wave corresponds to a large quantity of energy that comes to concentrate around the breathing frequency, presenting a particularly visible peak on the power spectrum (see figure 22). This energy peak only reflects the influence of breathing on cardiac activity and in some cases it can significantly disrupt and alter frequency-domain indices of HRV analysis [108,110,111].

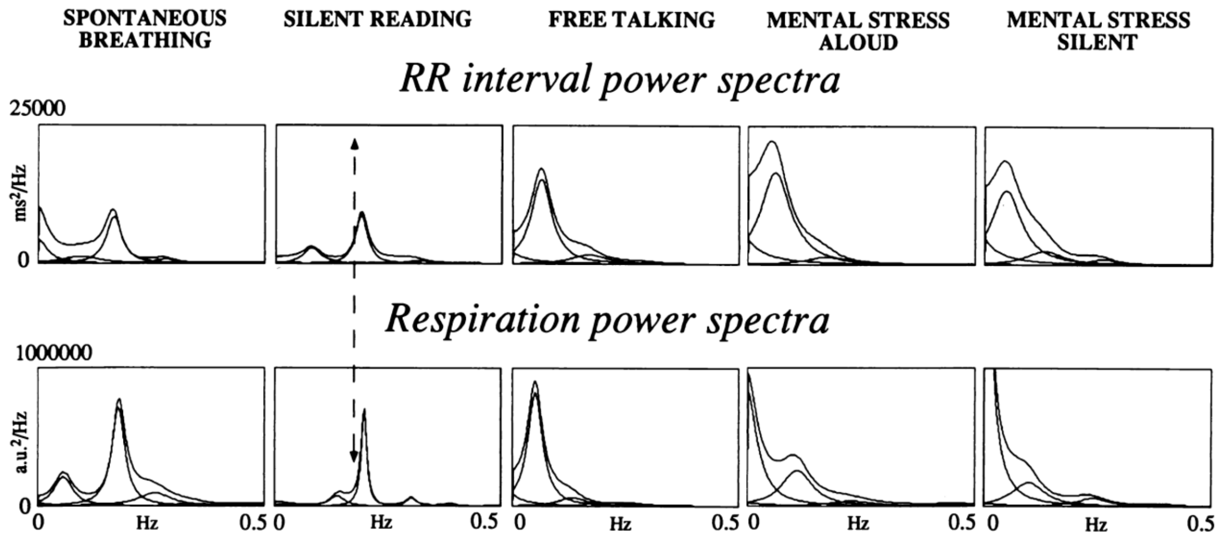

Figure 22: Power spectrum of RR interval and respiration obtained during several different activities of a subject [108].

We can observe that there is an increase in LF power in RR-intervals during free talking because of slowing of respiratory frequency. Therefore, we can expect that:

- During sympathetic activity or slowing of respiration rate, due to the increase in LF power, LF/HF ratio will be increased as well [108].
- Conversely, when a parasympathetic activity prevails or the respiration rate increases, LF component of spectrum decreases, and reduction in LF/HF ratio will be noted [108].

When at rest, a subject generally has a respiration rate frequency close to 0.16–0.33 Hz, or 10-20 breaths/ minute [109]. Nevertheless, it has been shown that under the effect of workload, the respiratory rate can decrease (4 to 10 breaths per min) and reach values close to 0.07–0.16 Hz [109]. When analyzing HRV in the frequency domain, we study the amount of energy present in the LF and HF bands with the frequencies which are respectively between 0.04 Hz and 0.15 Hz and between 0.15 Hz and 0.40 Hz. Thus, depending on the respiratory rhythm that we adopt during recording, we can artificially increase the respiratory sinus arrhythmia, the spectral power of LF and HF [108,110,111] . Based on this observation, many authors have attempted to measure the impact of the respiratory rhythm on the measurement of cardiac variability and in some publications, a comparison is made between spontaneous breathing and different controlled breathing patterns [108,110,111].

After studying the literature on this topic, we can notice that some indices of HRV are closely related and dependent on the respiration frequency of the individual during recording. In order to increase the reproducibility between measurements taken from one day to another, some studies have proposed to control this interaction by always imposing the same respiratory rate during the measurements [108].

Additionally, this method can facilitate quantitative comparisons by reducing interindividual differences since each subject follows exactly the same model of respiration. Despite everything, this solution remains controversial since all the authors are not necessarily in agreement with the frequency of respiration to be imposed [110]. Moreover, even in the event of consensus, there would remain a major obstacle which was clearly discussed in some leading studies. Indeed, it turns out that each subject does not react identically by following an imposed breathing pattern and it would seem that these differences are directly linked to the frequency of free breathing and the imposed breathing frequency specific to each subject [110].

Some studies have shown that the slower the imposed breathing frequency and the further from the subject's free breathing rate, more respiratory sinus arrhythmia is marked [110]. Note that the inverse relation is also true (i.e. the higher the frequency of controlled breathing and away from natural rhythm, a decrease in sinus arrhythmia is marked) [110]. For example, imposing a breathing frequency of 4-6 breaths per minute reduces the HR compared to the breathing rate of 14 breaths per minute [110]. In a study on this topic, out of the induced respiratory rates of 3,4,6,8,10,12, and 14 breaths/minute, the highest HRV was reached by 4 breaths/minute (see Figure 23) [110]. Therefore, imposing a slower respiratory rate produces a higher amplitude of HRV, whereas,by forcing a faster respiratory rate, lower amplitudes of HRV is observed.

In another study focusing on effects of respiration rate on short-term HRV, it was proven that HRV altered up to “33 % in SDNN, 37 % in RMSSD and 75 % in pNN50 between the different respiration rates. LF power differed up to 72 % ($p < 0.10$), HF power up to 36 % and R up to 48 %” [111]. It is also suggested to rely on the SDNN parameter for HRV analysis due to the large variations on the RMSSD and pNN50 indices [111].

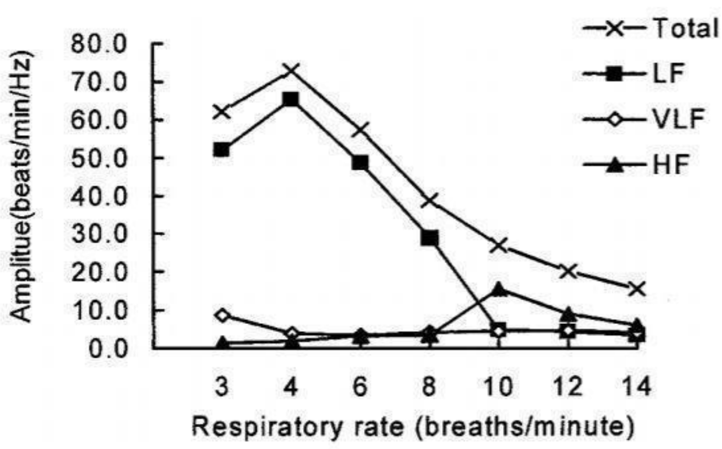

Figure 23: The amplitude of HRV at each induced respiratory rate [110].

From all above mentioned works, we can conclude the effect of respiration rate on HRV analysis as:

- An increased respiration rate causes a decrease in HR, an increase of LF component and LF/HF ratio [110].
- A decreased respiration rate results in an increase in HF component, a decrease in LF component and LF/HF ratio of HRV [110].

To conclude, whatever the method (free or controlled) of respiration and the frequency of respiration, respiratory sinus arrhythmia can significantly disrupt the frequency-domain indices of HRV recording and it appears it is necessary to take this influence into account in each of our measurements. Because of this reason, during our measurements we have let the ECG data to be recorded when our subjects were following a neutral frequency of breathing without applying any controlled breathing methods.

3.3.4 Sleep

Although the influence of sleep has already been discussed in previous chapters, here we aim to discuss the changes in HRV that can be observed during sleep. As we know from the previous chapters, in healthy individuals sleep is characterized by after 3 to 5 cycles lasting an average of 90 minutes. Each of these cycles is characterized by 5 distinct phases, the first 4 of which correspond to sleep at slow waves (Stage 1 or “light sleep”, stage 2 or “early sleep”, stage 3&4 “Orthodox/slow wave sleep”, stage 5 or “paradoxical/REM sleep”) which is also referred as non rapid eye movement sleep (NREM) then the last corresponds to rapid eye movement (REM) sleep[6].

The studies agree that a transfer of the sympathovagal balance occurs during the phase of slow wave sleep with sympathetic dominance which gradually decreases in favor of parasympathetic dominance. Conversely, the last phase (REM sleep) is characterized by sympathetic dominance similar to the waking period preceding falling asleep [112,113].During a study that focuses on the effect of stress on HRV during sleep, it was revealed that psychophysiological stress is highly correlated with poor levels of parasympathetic activity during NREM and REM sleep.Similarly, during REM sleep a high level of sympathovagal balance has found to be associated with the stressed condition of the subject [113].

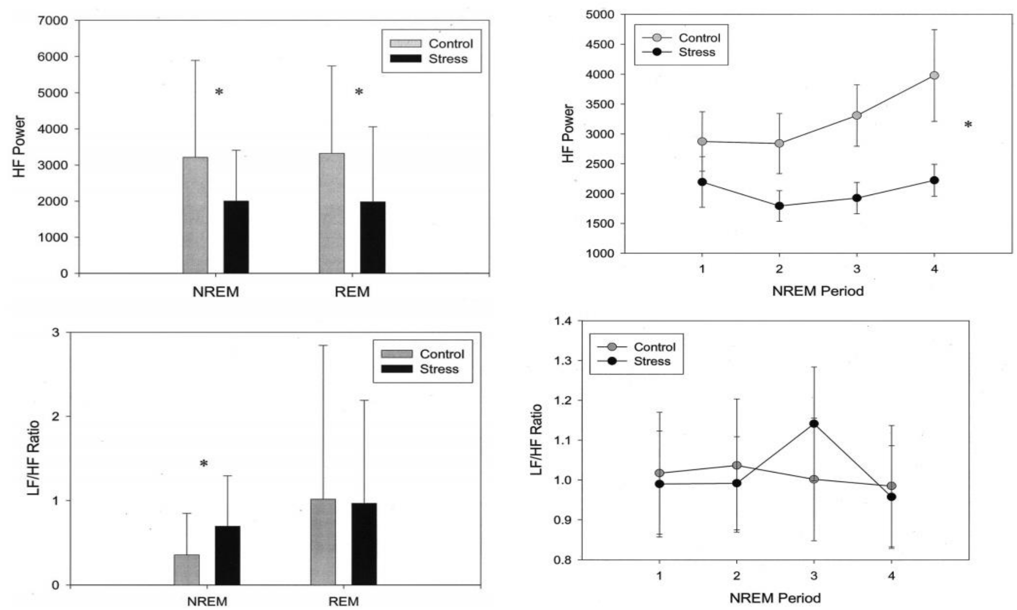

Figure 24: Analysis of covariance for all-night power in HF band and LF/HF ratio [113].

As can be observed by the results of the analysis, we can agree upon these facts:

- Stress experienced by a subject during sleep is associated with decreased PNS activity and increased sympathovagal balance (LF/HF ratio) during each single REM period. It is also related to the constantly changing profile of PNS activity throughout the night period [113].
- High levels of sympathovagal balance during NREM sleep can be related to small but evident decreases in sleep maintenance (reflection of the amount of wakefulness during sleep) [113].

3.3.5 Other factors

Food

Although the influence of diet on HRV is not often considered in HRV-fatigue related literature, it seems that there are studies which concentrates on this topic [114,115,116].In fact, after ingestion of food, there is a redistribution of blood towards the digestive tract to respond to the demands created by digestion. Evidently, there is an increase in the sympathovagal balance which appears to be attributed to the increase in sympathetic activity and to a decrease in vagal activity within one hour of digestion [114].

It seems that this acute cardiovascular response is multifactorial and depends on the type of food, its energy composition, the amount and when it is ingested [115]. More broadly, we can note that some long-term modifications of ANS activity can in part be attributed to specific diets. Thus, an increase in carbohydrate intake has the effect of stimulating sympathetic activity while a reduction in lipid intake has the effect of increasing parasympathetic activity [115].

Surprisingly, drinking pure water does not seem to have any significant effect on the various indices of HRV [116].On the other hand, many drinks containing substances of the alkaloid family have a significant psychotropic stimulant effect on the ANS, because of this reason, the absorption of coffee has the effect of increasing both sympathetic and parasympathetic activity [116]. Despite all, it is interesting to note that the psychotropic effect seems less pronounced in subjects accustomed to consuming coffee daily [116].

Conclusively, we can see that the ingestion of a meal or a simple caffeine-based drink has significant effects on the heart variability. Thus during our measurements the subjects were allowed to consume caffeine-based drinks and heavy meals.

Dehydration

At rest, a state of dehydration leads to a reduction in plasma volume and redistribution of blood to the skin to maintain the body's core temperature [117]. The cardiovascular system is then strongly called upon to respond to this lack of water. Thus, under conditions of advanced dehydration, it is possible to observe heart rhythm disturbances. Specifically, losses of water levels of the order of 2.5% of body weight are sufficient to significantly increase the HR values [117].At the same time, we can observe a drop in overall activity of the ANS.Besides, since we are interested in the PSD, it is interesting to note that, in dehydrated subjects, a much of the sympathetic energy is redistributed in the HF band [117].

Moreover, this influence of the parasympathetic branch has the role of reducing the effect of stress induced by dehydration [117]. Therefore, we can conclude that the subject must necessarily be in a state close to optimal hydration (euhydration) so that the various indicators of cardiac variability are not not affected. As a rule of thumb for regular HRV measurements, it is recommended to make comparisons of different records only when the subject's hydration level is similar, especially if the measurement is taken in the morning since during the night water losses are substantial.

Age and gender

During the previous studies on healthy individuals between the ages of 20 and 70, it was discovered that age and gender plays a factor in HRV values. HRV decreases with age and it has a greater variation in women than in men [92,118]. The value of HRV is influenced by physiological factors such as maturation of the sympathetic system. We observe an evolution of the sympathetic system with age, which could be one of the reasons for the change in HRV. During studies done, HRV has found to be decreasing with aging, and together with the increased risk of mortality, HRV may decrease to below levels [118]. HRV for all measures are lower in females than male subjects for subjects who are younger than 30 years [118]. For subjects who are older than 50 years these gender differences were not observed [118]. Specifically, the consensus on the literature is that the global variability, represented by the SDNN time index or the total signal strength, decreases significantly with age [118].

Because of this reason, for our measurements we selected the subjects in the same age range (23$\pm$2 years) and mostly from the same gender. Therefore, 8 subjects (7 men and 1 woman) between the ages of 21-25 years were chosen.

Local atmosphere during measurement

Within this section, we try to group the different parameters, constituting the local ambience and the atmosphere in which the subject finds himself when performing the measurements, which can influence or disrupt the measured recording of HRV.

First of all, changing the ambient temperature will modulate the activity of the ANS, via triggering of the thermoregulatory centers present in hypothalamus, to induce either vasodilation and sweating in case of heat, or vasoconstriction and chills in case of cold [119]. Thus, increasing the temperature of the medium in which the subject evolves from 3° C to 17° C reduces the overall activity of the ANS when being exposed to change in temperature[119].LF/HF ratio that demonstrates the sympathovagal balance significantly decreases as the ambient temperature is decreased [119].Therefore, we can say that it is mainly the parasympathetic activity which decreases without modifying sympathetic activity.

Secondly, in humans light can also cause acute physiological effects such as stopping melatonin secretion and increasing alertness [120]. So, the intensity and the light environment modify the activity of the ANS with an increase in the standard deviation of the RR intervals (SDNN index) when the individual performs the recording in a lighted room (10.000 lux) compared to a very dark environment (<0.01 lux) [120]. Additionally, LF/HF ratio increases with exposure to bright light or to extreme darkness, while dim light (100lux) does not have an effect on the ratio [120]. We can also note that even the color of the ambient lighting can influence the markers of the HRV since, compared to white light, exposure to a red or blue light significantly modifies the frequency and time indices[121].

Thirdly, since music can have an exciting or relaxing effect, it is interesting to consider the sound environment that surrounds the individual during the measurement. During previous studies differences have been reported depending on the type of music listened to (soft-classical music) and its influence on the HRV parameters [122]. Listening to soft music such as piano will have the effect of increasing the HF component of the signal spectrum of the HRV [122]. Conversely, a sound of mechanical origin, which can be considered as a harmful noise, will inhibit the parasympathetic nervous system which,therefore, will significantly increase the LF / HF ratio [122].

Finally, we can also mention among external influencers the evidence of a significant relationship between the quality of the air we breathe during recording and activity of the ANS [123]. It is proven that the major air pollutants such as: PM2.5, particle number concentration, black carbon, ozone, nitrogen dioxide, sulfur dioxide, carbon monoxide, in the recording room have a significant decreasing effect on the HRV indices [123]. With the elevation of $PM_{2.5}$ and Ozone levels in the room, SDNN and RMSSD parameters were found to be decreased [123]. The LF/HF ratio was increased by 18.6% per 8 μg/m^3 increase in 48-hr $PM_{2.5}$concentration in the recording room [123].

Overall, the different results of this part show us that during a series of measurements of heart variability, it is essential to strive to control as many parameters as possible that can influence the indices. From these previous studies we conclude that the room where the recordings are made must necessarily maintain a stable atmosphere (brightness, temperature, destructive noise-free, pollutant-free).

Cognitive activity and emotions

During a study, in order to stimulate the cognitive activity of subjects,the researchers asked the subjects to perform a mental calculation (subtraction) which has the effect of increasing sympathetic activity when the calculation is performed by a high voice [108]. On the other hand, when the calculation is performed in silence, it is rather the parasympathetic activity which tends to collapse [108]. Talking affects respiratory frequency in a way that it is shifted into the LF band which causes increasing LF%, decreasing HF%, therefore, increasing the LF/HF ratio [108]. Therefore,the increase in sympathetic activity would rather be attributable to the fact of stating the result calculation aloud and would obscure the effect directly linked to mental calculation which causes a decrease in vagal activity. We can expect to see this effect on HRV results, for instance, at the time when a pilot has to respond to the ATC instructions or request clearances and fly the simulator at the same time.

We can say that any cognitive activity can have a significant effect on the indices of the HRV. For example, some parameters (change in SDNN) are even used in mental imagery studies to determine whether the subject correctly performed his imaging task [124]. Mental imagery has the effect of reducing HRV[124]. This leads us to think that when measuring heart variability of pilots, we could encounter influences of the subject's conscious or unconscious imagining on the results due to the mental activity of the subject during the recording (positive or negative mental imagery at the instant present).

Other studies have measured the influence of emotional activity on HRV. By broadcasting images or specific music, they created very distinct emotions in the subject (fear, happiness, sadness) [125]. From these studies we can derive that negative emotional situations lead to a strong increase in the sympathetic activity whereas the positive emotional situations involve an increased activity of both branches of ANS [125].

In view of our methodological framework, we must discuss more specifically the effects of anxiety on indices of heart variability. Indeed, when performing an approach and landing at an unfamiliar airport, it is very common for the pilots to become anxious, which can cause immediate changes in the activity of the ANS. More specifically, during a study it was noted that vagal modulation of heart rate is sensitive to the recent anxiety and emotional stress regardless of a subject's attitude towards experienced anxiety [126].

In conclusion, these results are of great interest to us since although our measurements are performed under conditions of calm and external stability, we cannot unfortunately control the inner stability (and therefore emotions) of the individual. Thus, there is a good chance that, in the context of regular longitudinal monitoring of the heart variability, some results are strongly influenced by cognitive activity and condition of the emotional level of the individual at the time of recording. After studying this chapter which explains the various factors influencing the HRV, to remain more pragmatic and objective, it seems essential to keep in mind and take into account these parameters previously described during our HRV analysis.

3.4 ECG Signal processing

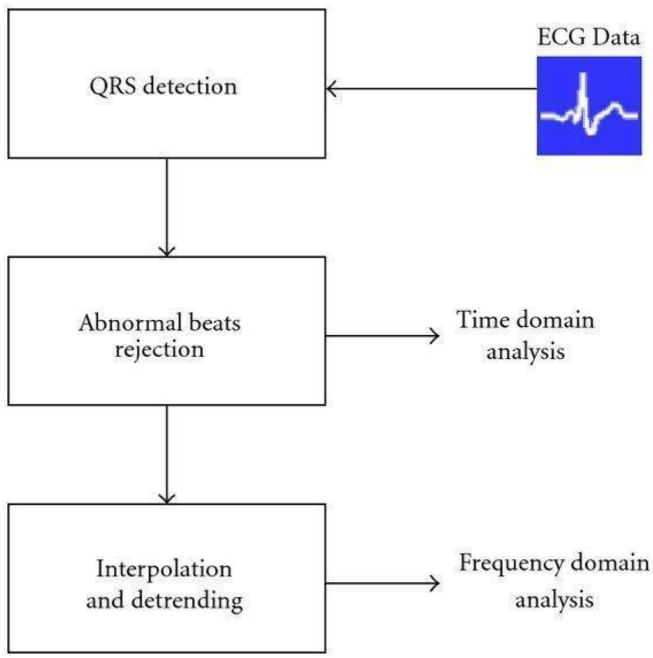

Figure 25: ECG signal processing steps [83].

On any electrocardiographic recording, there may appear unwanted items that interfere with the ECG signal and reduce it's high resolution. In practice, these disturbances in the ECG signal, specifically in the RR series, induce sudden variations of very low duration commonly referred to as artifacts or noises. Artifacts in an RR series can cause successive erroneous samples [65]. For these reasons, in order to obtain correct information and perform a proper diagnosis, it is essential to eliminate these artifacts before commencing HRV calculations.

3.4.1 Disruptions in ECG signal and the filtering methods

The disturbances causing artifacts in the RR series can be physiological (skin, muscle, breathing, etc.) or environmental (main current, electromagnetic interference, electrode placement etc.) caused. For instance, too much variation in the baseline can make it impossible to discern an anomaly such as over or under shifting of the S-T segment of an ECG wave.

Some of the types of these artifacts or also referred as “noises” you can see on an ECG include :

3.4.1.1 The baseline drift

The isoelectric line of the heart is called a baseline,and it corresponds to the trace that would be observed on an ECG if the heart had no electrical activity. The figure 26 shows an example of baseline drift on an ECG. This process is also known as baseline wander correction represented with the abbreviation “BW”.

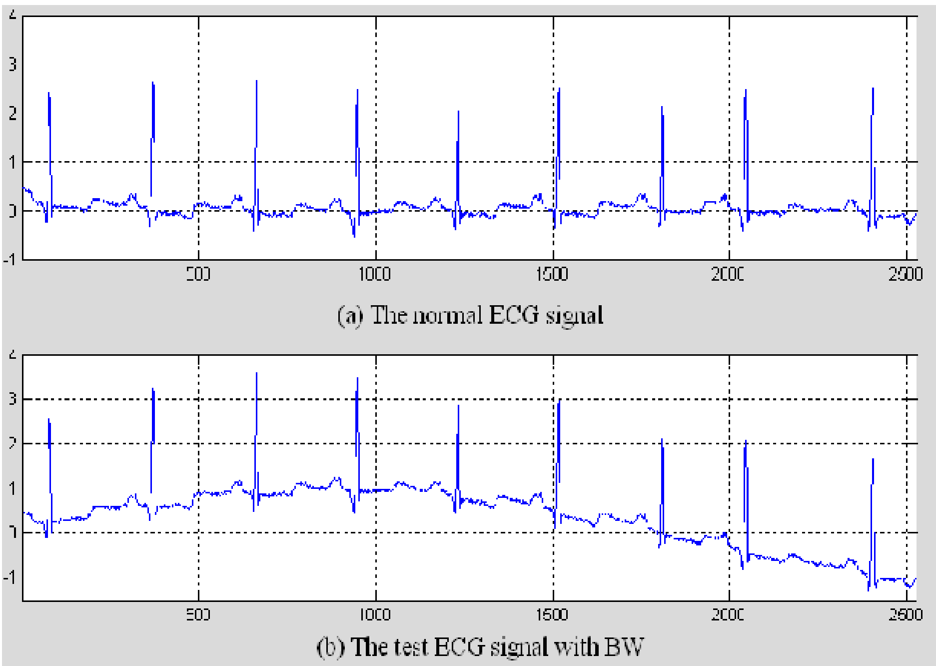

Figure 26: An ECG signal where baseline drift is eliminated (the 1st signal) vs. a signal without baseline drift elimination [127].

When the ECG is performed when the subject is stationary, this line is generally horizontal because the patient is not making any movement. Additionally, when the measurement takes place in a silent room this signal is less disturbed by outside noise. On the other hand, when a physical load is exerted on the subject such as the need to extend the landing gear or reach out for certain switches in the cockpit, the subject's movements modify the relative positions of the electrodes, therefore, this line presents a wave pattern such as indicated in the (b) condition. The baseline is physiological type of disturbance due to various factors such as: pulmonary ventilation, sweating (which changes the impedance of skin contact with electrodes), or involuntary movements of the subject which may result in occasional pauses in skin-to-electrode contact [127].

The baseline is taken as a reference to study the shape and height of the different heart waves; however, for the purpose of automatic processing of such a signal, it is imperative to identify it precisely in order to set the "zero" reference line. The elimination of this baseline is necessary to limit the morphological deformations of the ECG waves.

The method to remove the baseline drift relies on high-pass filtering, generally based on finite impulse filters [127]. For our ECG data, we will use the Pan and Tompkins algorithm on the MATLAB environment to remove this and some other below mentioned artifacts from our ECG data. The way how Tomkins algorithm works will be explained in the following chapter.

3.4.1.2 Interference of a 50 Hz signal

Generally, the signals are marred by noise linked to the electrical network. In the Czech Republic and most of the European countries, there is an alternating current of voltage 220V in the frequency 50Hz. This frequency is the cause of the main noise in the signal. It is found in all kinds of electrical devices and is therefore always detected. This noise can cause errors in the search for specific frequencies, therefore, there is a necessity to filter this noise. An example of an ECG modified by this type of noise is shown by the figure 27. This type of disturbance is difficult to avoid despite shielding of the cables connected to the electrodes.

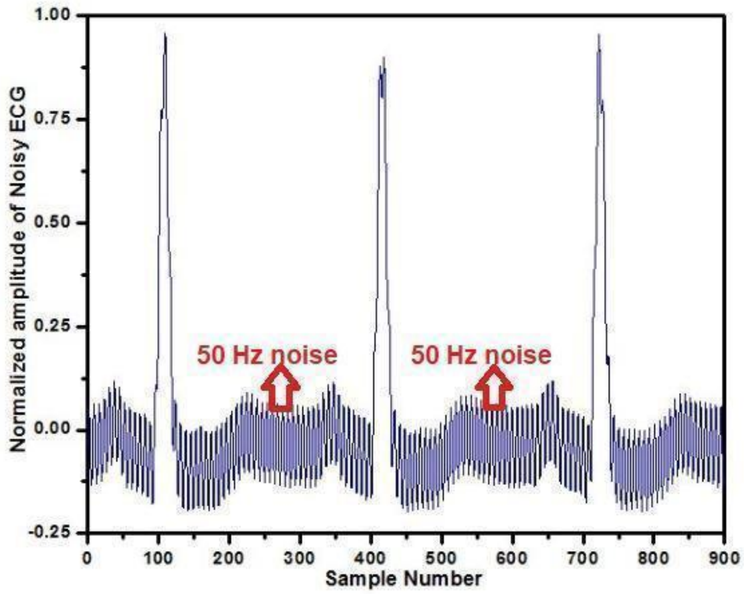

Figure 27: ECG signal with 50Hz noise artifact [128].

This type of disturbance is characterized by a sinusoidal signal of 50 Hz usually accompanied by a few harmonics. A simple method to reduce this type of noise is to use a filter to eliminate a particular frequency or a fine range of frequency components [128]. We will accomplish this by using the high pass filters in the Pan and Thomkins algorithm on the MATLAB environment which will remove this artifact from our ECG data.

3.4.1.3 Electromyographic interference

This type of noise corresponds to a type of disturbance of biological origin depending on the subject.

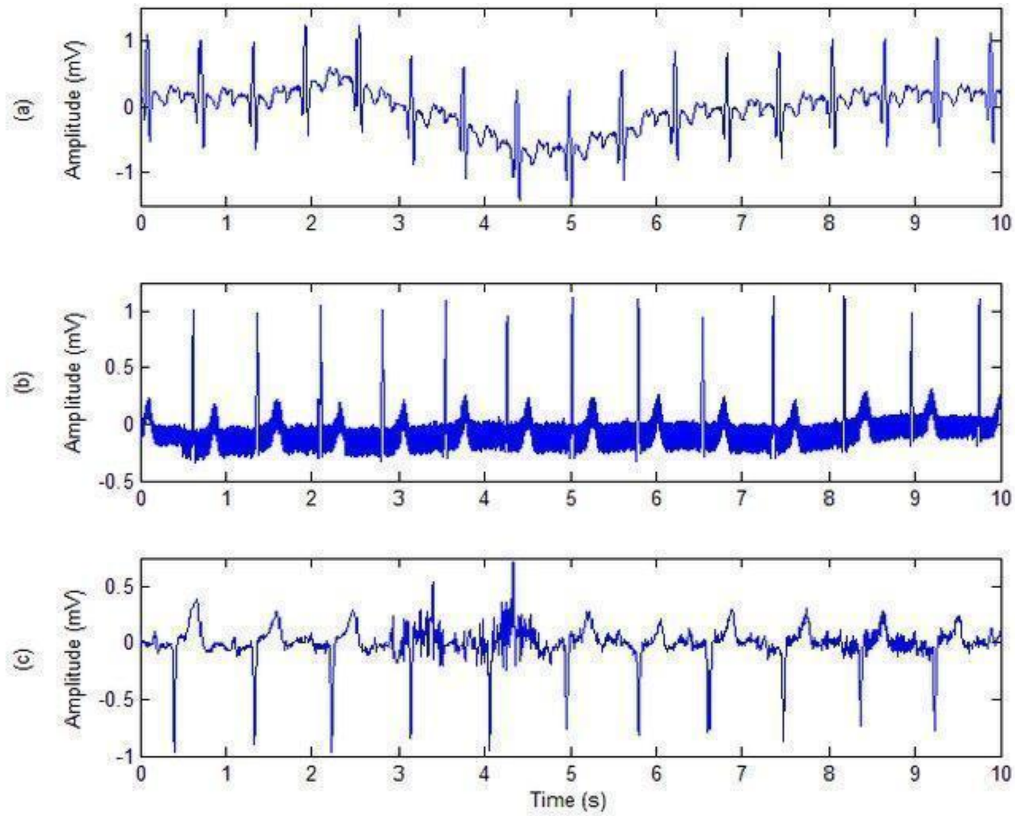

Figure 28: Common types of noise in ECG recordings. (a) Baseline wander (b) 50 Hz power line interference and (c) Electromyographic noise [65].

The condition (c) on the figure 28 shows that movements of the subjects can modify the signal resulting in difficulty in measurements where the subjects do not remain still and at rest. This EMG noise presents itself immensely and the components of the EMG noise frequencies can be found throughout the bandwidth of interest, overlapping the frequency band of the ECG signal [65].This type of artifact can also be removed by the 15 Hz low pass filter followed by 5 Hz high pass filter of the Pan and Tomkins algorithm as we wilI later.

3.4.2 Detection of the QRS complex

The goal of the detection algorithm is to develop comprehensive measurements of HRV where the detection of QRS complexes is of paramount importance in the analysis of ECG signals. Automatic detection of QRS complexes is difficult due to the morphology of these complexes which varies from one subject to another, and even in the same subject, it varies from cycle to cycle. Besides, even artifacts explained above and disturbances in various signals such as P and T waves can have similar characteristics to those of QRS complexes. Therefore a usage of a detection algorithm to arrange the ECG signal into an orderly manner is required before performing the HRV analysis.

Most of the detection algorithms proceed in two stages: a first stage in which the signal passes through a bandpass filter which removes noise and P and T waves. Then, the signal undergoes a nonlinear transformation, for example, the derivation to identify the steep slopes around the R wave, and the elevation squared to quantify the energy of QRS complexes. The second step is to make a decision based on threshold criteria. There are several QRS complex detection algorithms existing in the literature such as Pan and Tompkins algorithm, Derivative based algorithm, Wavelet transform based QRS detection and many more. However, because of its complexity and possible implementation into embedded systems, Pan and Tomkins method is usually preferred [129].

3.4.2.1 The Pan and Tompkins algorithm

Pan and Tompkins have developed a robust algorithm for the detection of the QRS complexes in single channel ECG data. This algorithm can be visualized as below:

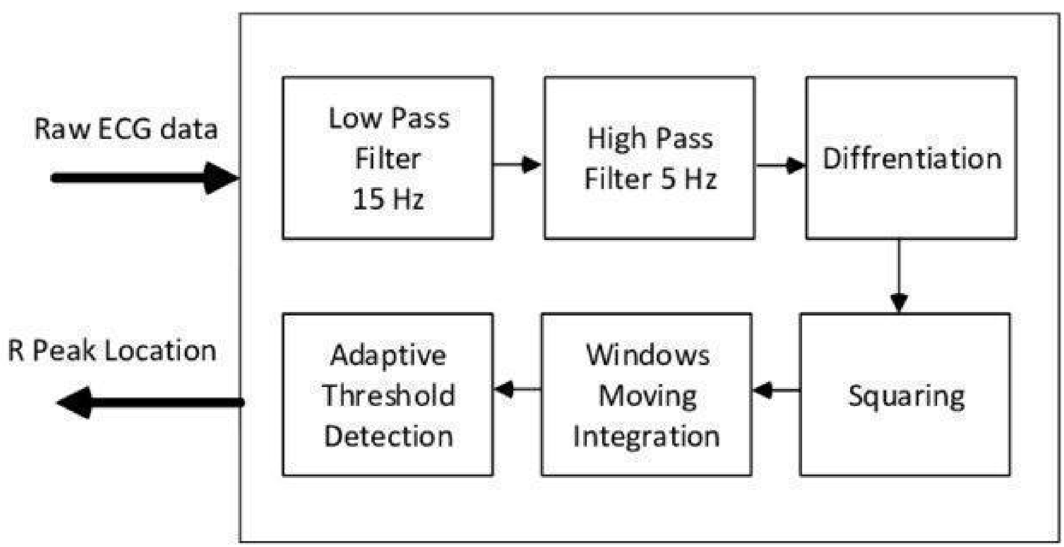

Figure 29: Pan and Thomkins algorithm as a model [129].

This algorithm proceeds with the following steps:

1. Low pass and high pass filters: 5-15Hz bandpass filter composed of a low-pass filter to remove high noise frequency (such as 50Hz grid interference) and a high pass filter eliminate low frequency components caused by respiration of the subject which is around 1 Hz. Transfer functions of low-pass and high-pass filters are relatively:

$$H(z) = \frac{(1-z^{-6})^2}{(1-z^{-1})^2} \qquad H(z) = \frac{(-1+32z^{-16}+z^{-32})^2}{(1-z^{-1})} \qquad [130]$$

2. Differentiation filter: The derivative circuit acts as a high pass filter. Since the QRS complex has the highest frequencies of the ECG, the derivative of these signals present the highest maximum values at these levels.
3. Squaring: The purpose of the square elevation is to distinguish between the R wave and the rest of the signal. The waves of small amplitudes and the negative parts are suppressed by remaining peaks of large amplitudes, which distinguishes QRS complexes.

$$y(nT) = [x(nT)]^2 \qquad [130]$$

   where T is the sampling period.

4. Windows moving integration: The integration of the signal makes it possible to obtain a unique maximum for each complex. The size of the integration window must be adapted to the average width of a QRS complex. If it is too large, the maximum is shifted in time with respect to the position of R (influence of the T wave). On the other hand, if it is too small, several peaks are obtained for the same size of the R wave, typically twice the mean width of a QRS complex.Windows moving integration corresponds to a filter whose output can be written as:

$$y[nT] = \frac{1}{N}(x[nT-(N-1)T] + x[nT-(N-2)T] + \cdots + x[nT]) \ [130]$$

where N represents the length of the averaging window. Therefore, we obtain an output signal which returns into 1 when a peak is detected, and is equal to 0 if there is no peak.

5. Adaptive threshold detection: At the end of the previous processing, the available signal has an absolute maximum for each QRS complex; it also has the opposite local maxima so-called the lowest amplitudes. This step therefore consists of a search for local minimas not taking into account the excessively lowest maximas which may correspond to the remaining noise that was not able to be removed by the low and high pass filters at the beginning of the process.

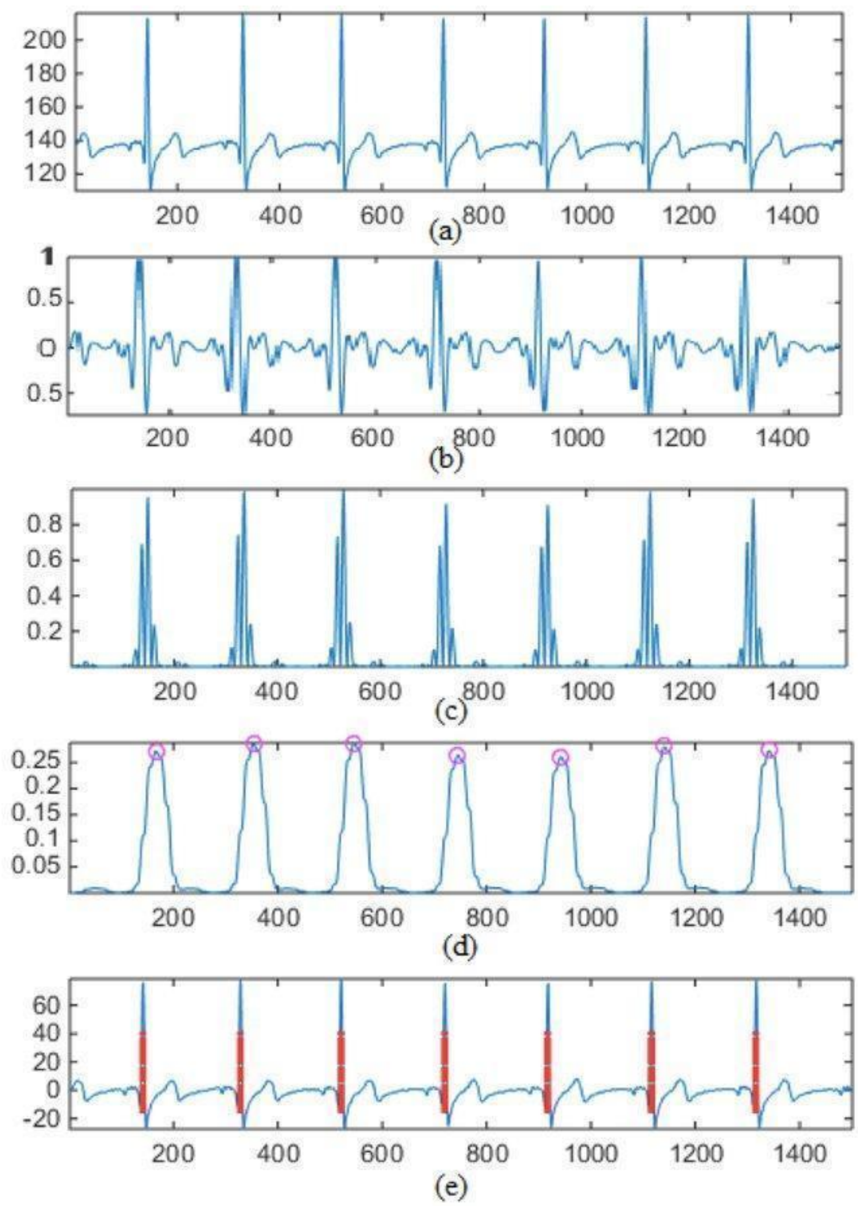

Figure 30: Illustration of QRS detection using Pan-Tompkins algorithm; (a) Raw ECG data; (b) ECG signal after band-pass filtering and derivation; (c) Squaring the data; (d) Integration and thresholding to detect QRS; (e) Pulse train of ECG signal [131].

For our case, we use a MATLAB code to apply the Pan Tomkins algorithm rather than using above mentioned formulas manually. All those formulas are embedded onto the MATLAB code. After applying Pan Tomkins algorithm, we are left with the locations of the R peaks of the ECG data which are then ready for HRV analysis. We perform the HRV analysis by using the HRV Analysis Software (HRVAS). This process will be explained further in the chapter 4.3 Data preprocessing.

3.5 Limitations of current state of the art

The pluralism of the methods to analyze HRV data and diversity of the HRV indices used in the fatigue related literature as we have discussed in chapters 3.2.4 and 3.2.5, is the main limitation of any study that deals with this topic. Absence of a standardized parameter which directly represents HRV makes researchers' job difficult by consuming their time while also calculating and evaluating other non-essential indices. Therefore, in this work, our primary goal is to find the most important and accurate HRV indices via linear regression model which could globally be used in pilot-fatigue detection studies, or perhaps in any fatigue related work. Measuring fatigue has challenged scientists for decades since there is no consensus in which of these measurements is the best and most accurate way to analyze fatigue behavior of a subject. Besides, an absence of a standardized measure and pluralism of the methods used in HRV studies as discussed earlier has limited efforts to advance our understanding about this issue. Therefore, we believe that, having defined indices to concentrate on would immensely assist a researcher by eliminating other redundant parameters. In order to contribute to removing this limitation from the literature, later we will apply a linear regression model to find out the most crucial parameters among all the indices mentioned in this chapter that represent fatigue on our pilot subjects.

4 Materials and methods

The aim of the measurement is to evaluate the change of the pilot's physiological condition when the subject is deprived from getting sleep and is in fatigued state during 24-hour measurements in which the subject performs several flying tasks. Subjects were connected to the ECG throughout the flying period and they were disconnected from the ECG only after landing and ending the measurement. Subsequently, they were acquainted with the measurement results by viewing the flight trajectory. Afterwards, the subjects completed a psychological test, a reaction time test and a short flight simulator questionnaire on a computer. The ECG data were autonomously saved and gathered in the device and subsequently made ready for performing statistical analysis to determine HRV indices.

4.1 Participants

The participating pilots were 3rd year students of the Professional Pilot major at the Faculty of Transportation Sciences, Department of Air Transport of CTU in Prague. Because of the effect of age and gender on HRV discussed under 3.3.5 Other factors, an attention was paid to select the subjects in the same age range (23$\pm$2 years) and mostly from the same gender. Therefore, 8 subjects (7 men and 1 woman) between the ages of 21-25 years were chosen. All the subjects were holders of an EASA issued private pilot license (PPL) and an EASA approved Class 1 medical certificate. When it comes to their airmanship, the subjects had a total flight time of around 100-150 hours, of which 30-40 hours were flown according to instrument flight rules (IFR). All of the subjects were in the stage of integrated ATPL (A) training at an approved training organization (ATO). Some of these subjects were in a phase of flight training according to IFR instruments on the FNPT II flight simulator, others had a rating on airplanes such as SEP IFR SPIC and were often performing IFR flights. The theoretical and practical experiences of the pilots were similar. The school flight simulator environment was almost new to everyone. Some had only some practical experience during the courses of radio telephony and radio navigation in the given simulator.

As we have studied earlier, mental imagery has the effect of reducing HRV. Because of this reason, avoiding mental imagery was advised to the subjects, and we kept in mind that during call-outs which were performed loud by the subjects, we could expect an increase in the LF/HF ratio due to the shift in the frequency of breathing as discussed before. Additionally, creation of distinct emotions through music or noise were prohibited, therefore, the measurements were performed in a silent simulator room to prevent influence of noise in HRV values. Change in HRV indices due to inner instability of the subjects could then be evaluated by using NASA TLX.

Besides, due to the effect of various food and drink types on HRV as discussed previously, the subjects were banned to consume caffeine-based drinks and reminded to drink adequate amounts of water to prevent negative influences of dehydration on HRV values.

4.2 Experimental set-up

Each of the 8 subjects were enrolled in the measurements and always 2 subjects participated in every 24-hours of measurement. Subjects were asked to wake up at 8:00, and to arrive at 17:00 in the building of the Faculty of Transport CVUT, where the measurement took place. Due to the effect of temperature, light and pollution on HRV parameters, the measurements were made in a room with an effective air conditioning that keeps the room temperature and air quality constant. Additionally, the effect of the subject's position on HRV results were considered as well. The movement data were collected using Motion Capture systems, afterwards, acceleration of a subject's body was processed from the data of repeated 24-hours measurements [132]. Since it is evident that the pilots could not maintain the same posture throughout the flights and disturbance of posture was required for several flying tasks (i.e. reaching out to the cockpit controls & switches, checklists and maps...) the data which was influenced by the negative effects of the body's acceleration were abandoned, and those were not used for HRV analysis.

The measurement began with a briefing at 18:00 where it was explained in detail to both subjects how to effectively use the navigation and on-board equipment, and where they got acquainted with the flight plan and maps. JeppFD software application on an iPad device made by the Jeppesen was used as an aeronautical map provider, which is widely used by the most large and small commercial carriers in the air transport industry. All subjects were familiar and they commonly used these types of maps to fly during their practical training, whether on a simulator or in an airplane. Standard instrument departure (SID) maps, standard instrument arrival (STAR) maps, instrument landing system (ILS) maps could be viewed on the iPad at any time on the pilot's discretion. In the JeppFD application, the subjects could compile the specified route and view its profile so that they could orient in flight direction.

Each flight lasted approximately one hour, the briefing before the flight took the pilot about 20 minutes.The flights took place on a simulator of a twin-engine propeller aircraft Beechcraft Baron. The cockpit of the simulator is equipped with standard flight, navigation and communication devices together with engine indicators. During flights emphasis was placed on utilizing the analog indicators: air speed indicator, artificial horizon, barometric altimeter, CDI, variometer, tachometer, turn coordinator & slip/skid indicator, direction indicator, VOR / LOC / GPS indicator, ADF indicator and a magnetic compass.

All flights took place in the territory of Germany. The departure and arrivals were made from and to the airports that have various radio navigation facilities and offered both precision and non-precision types of approaches. The airports' ICAO designators were: EDAC, EDBC, EDDC, EDDE, EDDT, EDOP, and EDVE. The flights never took-off or landed at the same airport, there was always a navigation flight that enabled landing to a different airport than departure. All flights took place under IFR conditions under the instrument meteorological conditions (IMC). The first subject started the flight on the simulator, while the second subject had about an hour and a half off, however, the second subject was not allowed to be present in the room on the simulator and observe the flight, and he was forbidden to sleep. Each of the flights therefore took place without the cooperation of multiple crew members.

The subject had a simulation of a real IFR flight on the simulator including receiving ATIS information, requesting start-up, taxi, take-off and landing requests and clearances. All these communications with the air traffic controller (ATC) were held in English. Additionally, the flights were flown like a usual IFR flight and the subjects performed read-backs to ATC and followed standard procedures such as: according to the specified permit setting the correct radio navigation and communication frequency, maintaining cleared altitude, using correct ICAO phraseology, briefing before landing, following the instructions of the controllers, position reporting and so on. In every flight, a certain strength and direction of the wind was set, which changed in direction and speed with change in altitude. The surrounding traffic and the communication with the surrounding traffic was not simulated.

The subject started each flight on the threshold of the runway in use. After getting acquainted with the route and the destination and receiving ATIS information, the cockpit was set and prepared for the flight with the simulator checklist. After obtaining the departure clearance from the controller in the instructor station of the simulator ,the subject initiated the take-off. During the enroute phase of the flight, the pilot followed the instructions of the controller and flew according to the cleared limits, contacted the ATC at reporting points and continuously checked the condition of the aircraft from available avionics equipment.

Each flight was completed by the ILS precision instrument approach. Meteorological conditions at the destination were set at the limit of the ICAO Category I precision approach minima so that there would not be an incentive to carry out the missed approach procedure. When the missed approach procedure was carried, it was due to other reasons such as: failure to obtain visual contact due to inaccurate piloting, the runway was occupied for some reason or the pilot did not get permission to land. The instrument approaches were selected so that their final approach section was relatively long (10 NM) in order to give enough time to the subject to bring the plane in a stabilized approach. By enforcing similar kinds of approach types in the same categories of the given ILS, the maximum possible comparability of the several pilots' performance is obtained. The pilot was connected to the ECG during the whole measurement on the simulator, where the cardiac and physiological activity were recorded.

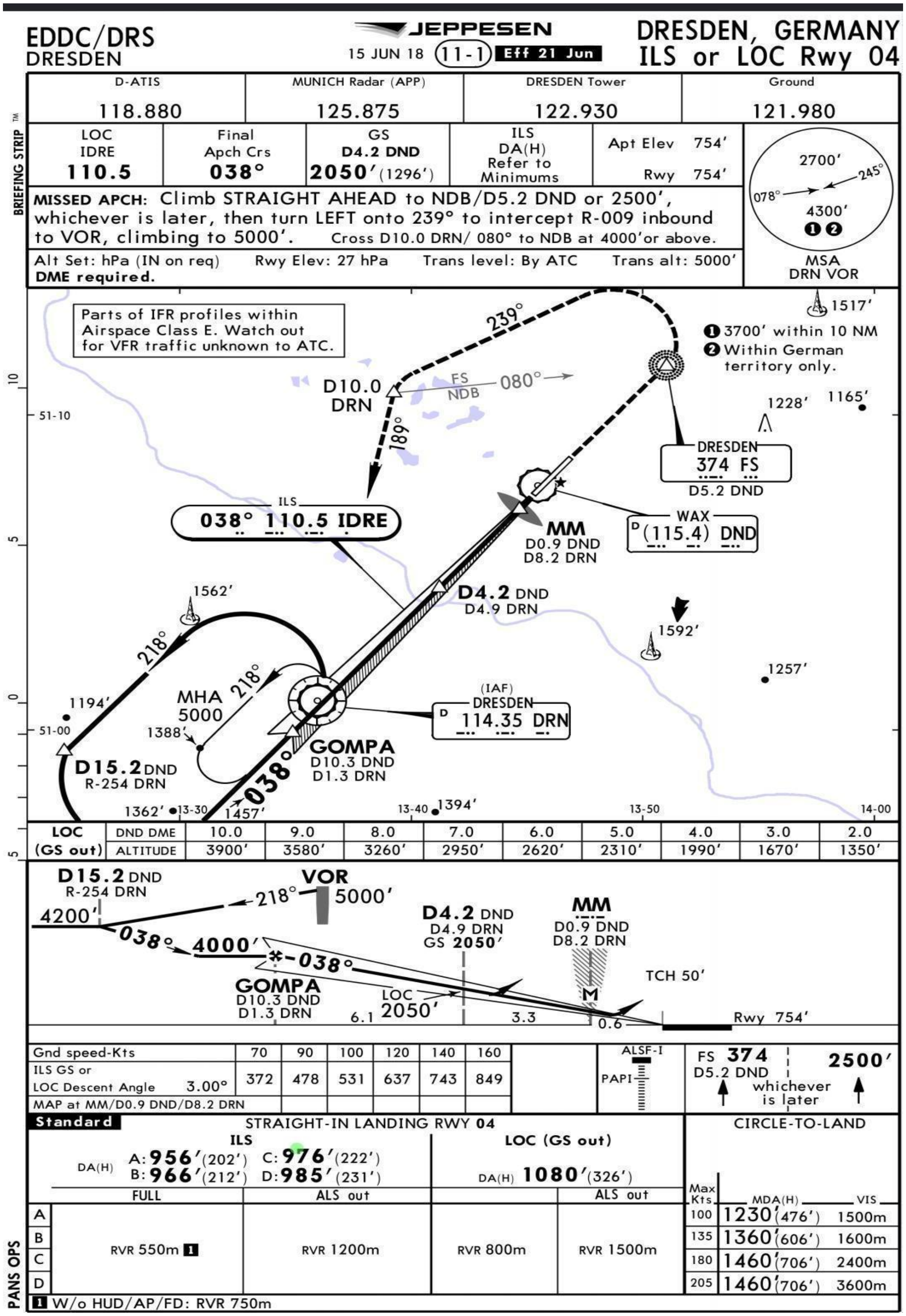

Figure 31: ILS approach chart for runway 04 of Dresden airport in Germany (EDDC) extracted from JeppFD application [133].

After completion of the first full landing, the pilot was again moved to the threshold of the runway and continued in the second part of the flight. Data collection was completed the moment the main landing wheels first touched the runway of the destination airport. Therefore, one flight consisted of two parts and lasted roughly an hour. Then the subject was disconnected from the sensor, exchanged with his colleague and took the tests in the next room. The entire flight, including the trajectory was saved after each flight for further processing. After the successful completion of the flight, the pilot was acquainted with the results of the flight. He was then allowed to look into the evaluation and to preview the trajectory of en-route flight or approach.

4.3 Statistical analysis

After determining the RR intervals by using the Pan-Tompkins method embedded in a MATLAB code, HRV Analysis Software was utilized for our HRV analysis [134]. HRVAS is an open-source free software application that offers to analyse HRV data. It is capable of detecting and filterining the IBI and it can perform various HRV analysis methods such as time-domain, frequency-domain, time-frequency, and Poincare plots [135]. After determining the R peaks on MATLAB, the time data is inserted on the HRVAS in microseconds units.

In order to find the most significant indices among all mentioned in the previous chapters, progressive regression method was used. This stepwise regression method that enables us to add or to remove the HRV indices according to their statistical importance to a multilinear model works in the following system: Firstly a regression model is constructed for the purpose of explaining the variance of several indices (dependent variables) using a combination of explanatory factors (independent variables). This model is designed so in a way that it answers the following question:

- What parameters are the most significant ones that can predict fatigue?

When a variable is added to the model , it assesses whether it is making a significant contribution, but also whether the one that contributed the least to the model remains significant. If not, the model removes it. In this way, it is possible to eliminate redundant variables. In every step, the p-value of an F-static is calculated for testing the existing models with or without a potential term. The hypothesis claims that the term would have zero coefficient once it is initially inserted to the model. The term is then added to the model if there is enough proof to reject the hypothesis. On the other hand, if a term is already in the model, the hypothesis states that the term has zero coefficient. Again, if there is not enough evidence to dismiss the hypothesis, the term is removed from the model [136].

We can explain the statistical models used in the following ways:

$$Observation_i \ : \ (Model_i \ ) + error_i \qquad [136] \quad (1)$$

Each value of the dependent variable ($Observation_i$) are explained in part by the statistical model. The part that the model is unable to explain is the specific error

($error_i$) associated with that value. In the case of multiple linear regression, this general model can be broken down more precisely as:

$$Y_i \ :(b_0 + b_1 X_1 + b_2 X_2 + \ldots + b_n X_n) + \varepsilon_i \qquad [136] \qquad (2)$$

Where Y represents the possible values of the dependent variable that can be explained by the regression model. Again, the portion that cannot be explained by the model is symbolized by ε_i which represents the error made by the model for each value of Y . We observe that each independent variable (X) is multiplied by its own beta coefficient (b) which in its standardized form corresponds to its relative contribution in the model. The constant (b_0) ,which is also called as the intercept, corresponds to the value of the dependent variable when all the independent variables are equal to 0.

This model (2) can also be written as a matrix in this way:

$$Y = Xb + \varepsilon \qquad [136] \ (3)$$

In this form, when Y is assumed as a vector in terms of n , X becomes a matrix in $n \times (t+1)$dimension with a rank if t+1, and b becomes the (t+1) vector that represents unknown regression coefficients [136].

r represents the number of terms which are deleted from model (1), meaning the number of coefficients which are set to zero [136]. Therefore, the number of terms which are kept in the final equation will be represented by $p = t + 1 - r$

Closely associated with the evaluation of the model, the multiple correlation index r^2represents the percentage of variance explained by the model (the contribution of independent variables).

This theory constitutes the basis of linear regression. According to the mathematical theory above, Initially stepwise regression on MATLAB was used to select specific parameters. In order to accomplish this the function *stepwisefit* was used. In every step, the p-value was calculated for testing the existing models with or without a potential term.

Initial columns included: none

Step 1, added column 55, p=0.000100207

Step 2, added column 12, p=0.000467908

Step 3, added column 76, p=0.0265291

Step 4, added column 82, p=0.0246784

Step 5, added column 43, p=0.0506788

Step 6, added column 54, p=0.0385919

Step 7, added column 56, p=0.0882483

Step 8, added column 34, p=0.021844

Step 9, added column 49, p=0.0249482

Step 10, added column 23, p=0.0533184

Step 11, added column 92, p=0.055475

Step 12, added column 62, p=0.0978375

Step 13, added column 69, p=0.0359382

Step 14, added column 11, p=0.0460104

Step 15, added column 68, p=0.0723128

Step 16, added column 6, p=0.0826263

Final columns included: 6 11 12 23 34 43 49 54 55 56 62 68 69 76 82 92

The stepwisefit display here shows that the columns 6,11,12,23,34,43,49,54,55,56,62,68,69,76,82, and 92 are included in the final model.

Coefficient	Std.Error	Status	*p*
[-0.0878]	[0.1030]	'Out'	[0.3955]
[-0.0687]	[0.1023]	'Out'	[0.5030]
[-0.0805]	[0.1831]	'Out'	[0.6609]
[-0.0893]	[0.1967]	'Out'	[0.6507]
[-0.0294]	[0.1224]	'Out'	[0.8107]
[0.1816]	[0.1036]	'In'	[0.0826]
[0.1480]	[0.1810]	'Out'	[0.4154]
[0.0227]	[0.0743]	'Out'	[0.7606]
[0.0890]	[0.0999]	'Out'	[0.3748]
[-0.1594]	[0.1032]	'Out'	[0.1252]
[-0.1927]	[0.0785]	'In'	[0.0157]
[0.4180]	[0.0858]	'In'	[3.8794e-06]
[-0.0175]	[0.1148]	'Out'	[0.8790]
[-0.0654]	[0.1506]	'Out'	[0.6647]

[0.0371]	[0.1497]	'Out'	[0.8047]
[-0.0521]	[0.1482]	'Out'	[0.7259]
[0.0035]	[0.1261]	'Out'	[0.9782]
[0.0231]	[0.1056]	'Out'	[0.8272]
[-0.0130]	[0.1615]	'Out'	[0.9360]
[-0.1020]	[0.2203]	'Out'	[0.6442]
[0.1020]	[0.2203]	'Out'	[0.6442]
[-0.0913]	[0.1941]	'Out'	[0.6393]
[-0.4446]	[0.2557]	'In'	[0.0850]
[-0.0224]	[0.0803]	'Out'	[0.7812]
[-5.0580e-04]	[0.0810]	'Out'	[0.9950]
[0.0152]	[0.1165]	'Out'	[0.8961]
[0.0014]	[0.1432]	'Out'	[0.9921]
[0.0567]	[0.1495]	'Out'	[0.7054]
[-0.0095]	[0.1503]	'Out'	[0.9497]
[-1.0296e-04]	[0.1132]	'Out'	[0.9993]
[-0.0268]	[0.1063]	'Out'	[0.8015]
[-0.0840]	[0.1807]	'Out'	[0.6430]
[0]	[0.7490]	'Out'	[1]
[0.2934]	[0.1405]	'In'	[0.0391]
[-0.0626]	[0.3783]	'Out'	[0.8690]
[0.3675]	[0.3400]	'Out'	[0.2822]
[-0.1184]	[0.0903]	'Out'	[0.1924]
[0.0460]	[0.0804]	'Out'	[0.5685]
[-0.0553]	[0.0772]	'Out'	[0.4754]
[-0.0400]	[0.1027]	'Out'	[0.6976]
[-0.0090]	[0.1210]	'Out'	[0.9410]
[-0.0710]	[0.0970]	'Out'	[0.4659]
[0.5107]	[0.1177]	'In'	[3.2761e-05]

[0.0327]	[0.1492]	'Out'	[0.8268]
[0.0736]	[0.1762]	'Out'	[0.6769]
[-0.0892]	[0.1581]	'Out'	[0.5740]
[0.0892]	[0.1581]	'Out'	[0.5740]
[-0.2320]	[0.1548]	'Out'	[0.1370]
[0.3047]	[0.0797]	'In'	[2.2261e-04]
[0.0671]	[0.0763]	'Out'	[0.3813]
[0.0661]	[0.0734]	'Out'	[0.3699]
[0.1468]	[0.1814]	'Out'	[0.4202]
[-0.0793]	[0.1742]	'Out'	[0.6501]
[0.1990]	[0.0781]	'In'	[0.0123]
[-0.4204]	[0.1456]	'In'	[0.0047]
[0.5733]	[0.1179]	'In'	[4.0582e-06]
[-0.2339]	[0.3338]	'Out'	[0.4851]
[-0.0406]	[0.1342]	'Out'	[0.7627]
[-0.0349]	[0.1506]	'Out'	[0.8173]
[-0.0336]	[0.1497]	'Out'	[0.8227]
[-0.0607]	[0.1520]	'Out'	[0.6903]
[-0.3107]	[0.0979]	'In'	[0.0020]
[0.0473]	[0.1605]	'Out'	[0.7686]
[-0.0875]	[0.2282]	'Out'	[0.7021]
[0.0742]	[0.2319]	'Out'	[0.7495]
[-0.0742]	[0.2319]	'Out'	[0.7495]
[0.0568]	[0.1973]	'Out'	[0.7741]
[0.2540]	[0.1251]	'In'	[0.0449]
[-0.1835]	[0.0804]	'In'	[0.0245]
[0.0543]	[0.0715]	'Out'	[0.4492]
[0.0704]	[0.0998]	'Out'	[0.4824]
[-0.0677]	[0.1446]	'Out'	[0.6406]

[-0.0803]	[0.1536]	'Out'	[0.6024]
[-0.0307]	[0.1590]	'Out'	[0.8473]
[-0.0993]	[0.1601]	'Out'	[0.5364]
[0.2715]	[0.0897]	'In'	[0.0031]
[0.0042]	[0.1678]	'Out'	[0.9801]
[0.0055]	[0.1684]	'Out'	[0.9739]
[0.0023]	[0.1697]	'Out'	[0.9890]
[-0.0023]	[0.1697]	'Out'	[0.9890]
[-0.0142]	[0.1729]	'Out'	[0.9348]
[0.2511]	[0.0929]	'In'	[0.0080]
[-0.0086]	[0.0865]	'Out'	[0.9208]
[0.0842]	[0.0751]	'Out'	[0.2651]
[0.0728]	[0.1020]	'Out'	[0.4768]
[0.0718]	[0.1062]	'Out'	[0.5003]
[0.1248]	[0.1330]	'Out'	[0.3499]
[0.1515]	[0.1295]	'Out'	[0.2448]
[0.1122]	[0.1297]	'Out'	[0.3891]
[-0.2543]	[0.2073]	'Out'	[0.2227]
[0.1347]	[0.1302]	'Out'	[0.3032]
[-0.2375]	[0.1357]	'In'	[0.0830]
[0.1361]	[0.3297]	'Out'	[0.6806]
[-0.1361]	[0.3297]	'Out'	[0.6806]
[0.0771]	[0.2516]	'Out'	[0.7599]
[0.0900]	[0.0991]	'Out'	[0.3663]
[0.0396]	[0.0931]	'Out'	[0.6712]
[0.0844]	[0.0901]	'Out'	[0.3507]
[0.0935]	[0.0766]	'Out'	[0.2250]

Then, the linear regression model of the dependency of the parameters that were obtained from stepwise regression was constructed. For this, the *LinearModel.fit* function on MATLAB was used.

mdl2 = LinearModel.fit(X,y) creates a linear model of the responses *y* to a data matrix *x.* Where *x* is the result of the stepwise regression matrix and the *y*:

y ~ 1 + x1 + x2 + x3 + x4 + x5 + x6 + x7 + x8 + x9 + x10 + x11 + x12 + x13 + x14 + x15 + x16

Estimated Coefficients:

	Estimate	**SE**	**tStat**	**pValue**
(Intercept)	1.8902	0.062948	30.028	1.1922e-53
x1	0.18161	0.10365	1.7522	0.082626
x2	-0.19268	0.078509	-2.4542	0.01575
x3	0.41801	0.085789	4.8725	3.8794e-06
x4	-0.44456	0.25568	-1.7388	0.084982
x5	0.2934	0.14046	2.0888	0.039117
x6	0.51074	0.1177	4.3392	3.2761e-05
x7	0.30474	0.079707	3.8233	0.00022261
x8	0.19895	0.078086	2.5479	0.012273
x9	-0.42036	0.14559	-2.8873	0.0047109
x10	0.5733	0.11792	4.8616	4.0582e-06
x11	-0.31066	0.09788	-3.1739	0.001969
x12	0.25396	0.12511	2.0299	0.044868
x13	-0.18353	0.080431	-2.2818	0.024499
x14	0.27145	0.089698	3.0263	0.0031076
x15	0.25108	0.092867	2.7037	0.0079903
x16	-0.23753	0.13572	-1.7502	0.082973

Number of observations: 123, Error degrees of freedom: 106

Root Mean Squared Error: 0.698

R-squared: 0.517, Adjusted R-Squared 0.444

F-statistic vs. constant model: 7.08, p-value = 8e-11

Mean-square testing error = 0.882630

Number of trees:

29 14

The next step is to define a random partition on our training sets for validating the linear regression model using cross-validation. The training x testing data is set to 30:70 by *cvpartition* function. Since we got multiple trees (boosted trees), in order for the classification and importance of parameters selected by stepwise regression the functions *RegressionTree.template* and *fitensemble* were used.

Number of trees after cutting-off

14

Decision tree for regression:

1 if Time Domain (pNNx)<-0.934223 then node 2 elseif Time Domain (pNNx)>=-0.934223 then node 3 else 0.549424

2 if Time-Freq- AR (pVLF)<-0.440202 then node 4 elseif Time-Freq- AR (pVLF)>=-0.440202 then node 5 else 0.319947

3 if Nonlinear (alpha)<-0.334425 then node 6 elseif Nonlinear (alpha)>=-0.334425 then node 7 else 0.597905

4 fit = -0.339188

5 if Time-Freq- AR (peakLF)<0.924232 then node 8 elseif Time-Freq- AR (peakLF)>=0.924232 then node 9 else 0.484731

6 if Time Domain (TINN)<1.95218 then node 10 elseif Time Domain (TINN)>=1.95218 then node 11 else 0.468387

7 if Time-Freq- Lomb (pVLF)<1.47327 then node 12 elseif Time-Freq- Lomb (pVLF)>=1.47327 then node 13 else 0.682243

8 fit = 0.677626

9 fit = -0.0939545

10 if Nonlinear (sampen)<-1.01118 then node 14 elseif Nonlinear (sampen)>=-1.01118 then node 15 else 0.408078

11 fit = 0.97096

12 if Time Domain (TINN)<-1.17344 then node 16 elseif Time Domain (TINN)>=-1.17344 then node 17 else 0.692201

13 fit = 0.263994

14 fit = -0.0581468

15 if Time-Freq- Lomb (pVLF)<-1.64511 then node 18 elseif Time-Freq- Lomb (pVLF)>=-1.64511 then node 19 else 0.524634

16 fit = 0.314856

17 if Time-Freq- AR (pVLF)<-0.271014 then node 20 elseif Time-Freq- AR (pVLF)>=-0.271014 then node 21 else 0.701404

18 fit = -0.314552

19 if Freq Domain- Welch (peakVLF)<0.433013 then node 22 elseif Freq Domain- Welch (peakVLF)>=0.433013 then node 23 else 0.568802

20 if Time-Freq- Lomb (pVLF)<0.377386 then node 24 elseif Time-Freq- Lomb (pVLF)>=0.377386 then node 25 else 0.769029

21 if Time-Freq- Lomb (pVLF)<-0.450501 then node 26 elseif Time-Freq- Lomb (pVLF)>=-0.450501 then node 27 else 0.648481

22 if Nonlinear (alpha1)<-0.461303 then node 28 elseif Nonlinear (alpha1)>=-0.461303 then node 29 else 0.627052

23 fit = 0.0736747

24 if Time Domain (HRVTi)<-0.37028 then node 30 elseif Time Domain (HRVTi)>=-0.37028 then node 31 else 0.709782

25 fit = 0.92307

26 fit = 0.922001

27 if Freq Domain- LS (peakVLF)<-0.998037 then node 32 elseif Freq Domain- LS (peakVLF)>=-0.998037 then node 33 else 0.622431

28 fit = 0.530902

29 fit = 0.73522

30 fit = 0.809506

31 fit = 0.550225

32 fit = 0.877259

33 if Time-Freq- Lomb (peakVLF)<0.176777 then node 34 elseif Time-Freq- Lomb (peakVLF)>=0.176777 then node 35 else 0.595607

34 if Freq Domain- AR (nHF)<-1.4025 then node 36 elseif Freq Domain- AR (nHF)>=-1.4025 then node 37 else 0.539598

35 fit = 0.691624

36 fit = 0.71383

37 if Time Domain (TINN)<1.62246 then node 38 elseif Time Domain (TINN)>=1.62246 then node 39 else 0.523759

38 if Time Domain (HRVTi)<-0.245181 then node 40 elseif Time Domain (HRVTi)>=-0.245181 then node 41 else 0.533662

39 fit = 0.424721

40 fit = 0.563498

41 fit = 0.513772

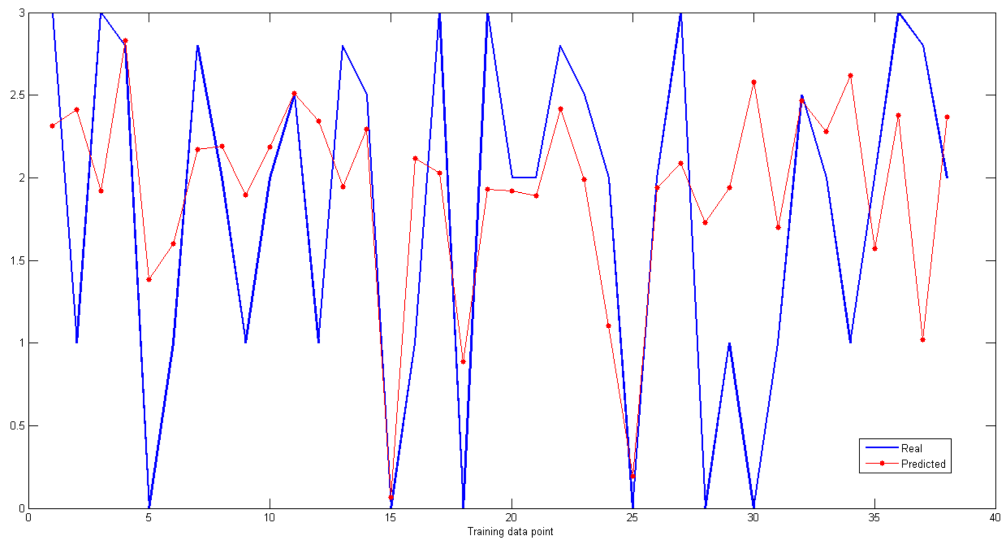

Figure 32: Classification and the ability of the classificator to predict the indices.

The above figure represents the classificator which was set to 30:70, and it shows how we are able to predict the data obtained during the measurements. This indicates that the classificator was trained to test 70% of the data obtained during real measurements and advance its machine learning contribution to the remaining 30% of the data.By this way, this machine learning system can validate and compare the relevancy of the indices continuously to the rest of the data.

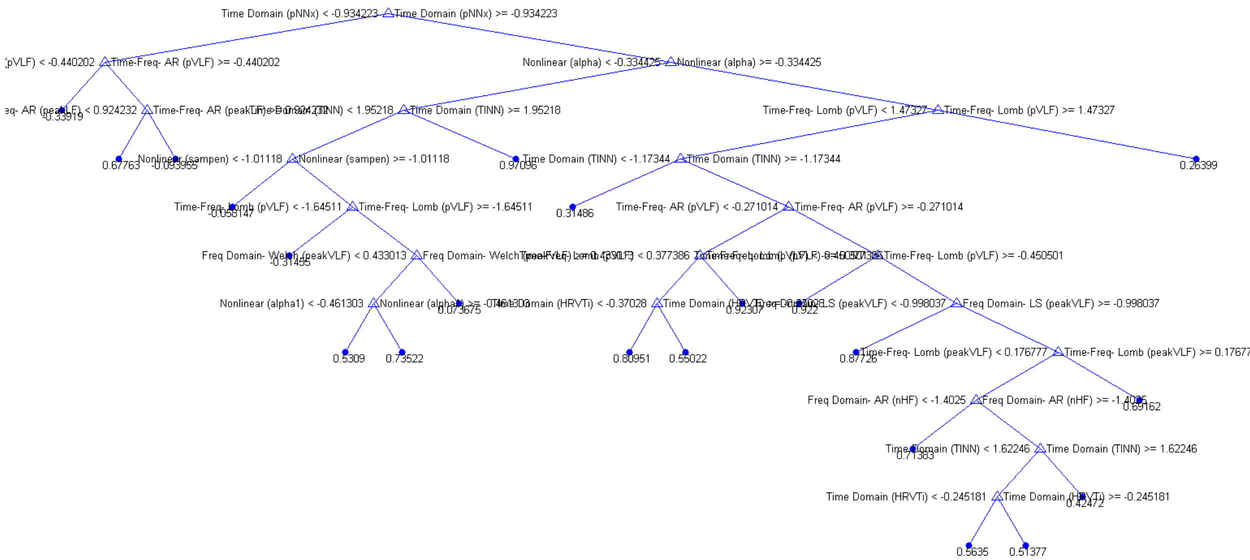

Figure 33: Decision tree for regression analysis.

This decision tree enables us predicting responses to the probability of the significance of an index. It is made out of several steps and in each step a value of one predictor variable has to be checked. It precedes with the following structure: During the first step, if for a certain time the measured pNNx value of a subject is less than -0.934223 then pVLF index hold a higher significance than pNNx, and while later continuing the regression, pVLF value should be considered instead of pNNx. On the other hand, if the pNNx value is higher than or equal to -0.934223 during the measurement, alpha index represents a higher significance rather than the old pNNx value and the following comparisons must be made by relaying on the alpha index. For the second step, if pVLF value is lower than -0.440202, the regression tree classifies the data as type -0.33919. However, if the pVLF value is higher or equal to -0.440202,then the parameter peak LF carries a higher importance compared to the pVLF index, and the regression tree classifies the data as type 0.67763 and -0.093955. At the end of the regression steps only the most significant indices and their corresponding data types are assigned.

5 Results

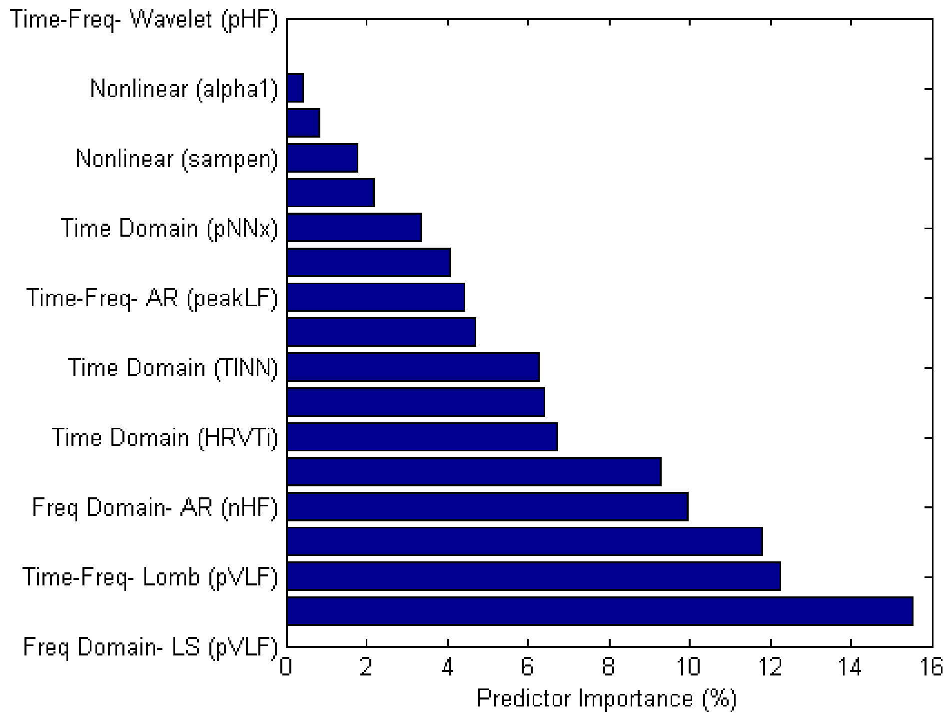

Figure 34: Importance of the HRV indices as a percentage of importance

According to the results, the most significant HRV indices to represent fatigue are:

VLF component by frequency-domain analysis has the predictor importance 15.5%.

VLF component by time-frequency domain analysis has the predictor importance 12.3%.

HF component by frequency-domain analysis has the predictor importance 11.8%.

HRVTi (Triangular index) by time-domain analysis has the predictor importance 7%.

TINN by time-domain analysis has the predictor importance 6.5%.

LF peak by time-frequency analysis has the predictor importance 5%.

pNNx by time-domain analysis has the predictor importance 4%.

SampEn by non-linear analysis has the predictor importance 2%.

DFA alpha1 by non-linear analysis has the predictor importance 0.5%.

6 Discussion

From these results, we can observe that the most significant indices of HRV analysis are mostly the indices derived from the frequency domain and time-frequency analysis mainly VLF and HF components of the power spectrum. Even though VLF component is not often considered in the HRV studies due to its complexity of interpretation, for our measurements it was revealed that it represents fatigued condition of a subject the most. HF component seems to be as well important. Providing that more than 10% of predictor importance is given, then we can say that values of VLF and HF components are more than enough to determine fatigue induced on the subjects due to sleep deprivation.

Based on these results, pVLF index of the frequency domain and time-frequency domain analysis and nHF parameter of frequency-domain analysis of HRV corresponds to the most important indices. It is interesting to see that the both of the non-linear domain analysis indices have less than 3% predictor importance. Also the parameters of the non-linear analysis SD1 and SD2 did not come out as significant, therefore a Poincare plot was not created. This gives us a clue that presentation of power spectrum is more significant than Poincare plot. This conclusion contradicts with the studies which claim that Poincare plot analysis is more sensitive at evaluating the sympathovagal balance than power spectral analysis of HRV [137].

It is also evident that the geometrical indices (HRVTi, TINN) play much more factor than indices from the statistical methods (pNNx) of time-domain analysis of HRV. Additionally, we did not encounter with the three of the most common HRV indices to assess pilot fatigue mentioned in the literature: SDNN, RMSSD, LF/HF ratio [13,19]. Especially, the absence of the LF/HF ratio among our list of the most significant HRV parameters was interesting to notice. This can be associated with the fact that the results of the regression analysis is not perfect. The classification of the indices should be more accurate, however, since we had only limited number of measurements and subjects, this hypothesis cannot be fully supported. Additionally, among the limitations of the regression analysis,we can mention that it was challenging to set which measurement corresponds to which specific level of fatigue.

Although this list of the most significant indices that our results came up with does not exactly correspond to the final indices used to evaluate pilot fatigue in other studies [12,13,14,15]; it represents a similar trend in a way that prevalence of VLF or LF components was generally utilized to assess the fatigued condition of the pilots.

For the future studies, in order to validate our hypothesis that VLF and HF components of PSD, and geometric indices of time-domain analysis constitute the most significant parameters, the number of measurements and exposed subjects must be higher. When it comes to the complexity of these measurements, the classificator could be improved by adding the indices from the other physiological measurements to the existing model such as EEG data, reaction time, blink rate, pupillary response time. This would enable determination of the most important indices among all physiological parameters.

7 Conclusion

Given the global growth in air traffic and the increasing safety trend and culture, there is a necessity to address human factors. The professional pilot job is usually associated with responsibility for the lives of a large number of people. The historical development of safety management has reached a stage where it is important to collect and analyze various data in order to prevent possible events, incidents and accidents, before they occur. For this reason, it is necessary to discuss, among other things, fatigue, and based on the results of studies, to take an appropriate position on it.

Based on the above, the aim of this bachelor thesis was to evaluate the physiological effects of fatigue on the results of HRV analysis, by monitoring the pilot subjects cardiac activity using an ECG device during continuous measurements. A single measurement lasted 24 hours and started at 18:00 LT. Each measurement was always attended by two subjects who were up from 8 o'clock on the day of the measurement. The first subject commenced a single-pilot flight according to IFR rules on a school simulator of a multi engine twin-propeller aircraft, Beechcraft Baron. Every flight lasted about 90 minutes including pre-flight preparation, the flight itself and the post flight analysis. Throughout the flight duration, the subject was connected to an ECG device which was capable of storing the cardiac activity data and transferring the data further to perform statistical analysis. After completing the flight, the subject moved to the next room, where, in conditions of complete calmness, the subject filled psychological questionnaires and tests. While the first subject completed questionnaires and underwent tests, the second subject began a flight on the simulator. During about 24 hours, 16 measurements were performed in total.

The bachelor's thesis initially describes the theoretical part of the history of the human factors in aviation and the leading studies done in the last century in this domain. It also describes the concept of fatigue, operational factors that lead to fatigue, consequences of it and safety systems taken to prevent it in the modern commercial aviation industry. Afterwards, methods of measuring fatigue, physiological measures of fatigue, and evaluation of HRV and HRV analysis methods to interpret fatigue is provided. The internal and external factors influencing the results of HRV were discussed and considered during the measurements. Elimination of the disruptions in the ECG signal and determining R peaks of the QRS complexes were accomplished by the Pan and Thompkin's algorithm embedded in the MATLAB environment. HRVAS tool was utilized for the HRV analysis. The values of the HRV indices from time-domain, frequency-domain, non-linear and time-frequency analysis, and Poincare graphs were obtained as a result. Eventually, linear regression statistical analysis was performed on the values of the HRV indices in order to determine the most significant parameters that represent fatigued condition of the pilot subjects.

The prevailing results of the linear regression analysis reveals that: VLF and HF components are the most important indices of HRV analysis that presents more than 10% predictor importance. We strongly believe that these results would be highly beneficial to the fellow academicians who deal with detecting fatigue based on cardiac activity, more specifically, HRV indices. Having a global set of the most significant HRV indices removes the confusion in the literature about the plurality of the parameters that is discussed in the chapter 3.2.5.

When it comes to the limitations of the measurements performed, we shall consider that there was a small number of measurements because of the limited number of the subjects who participated in the experiment. Unfortunately, for the purpose of prevention against dissemination of Covid-19 infection, the measurements could not be repeated enough times according to the original plan.

Secondly, during the process of the measurements we also have encountered problems with the data collection itself. Occasionally, there were sometimes where the ECG data was not saved or missing. Results further may be distorted by the fact that there was an effort to adhere to the time schedule. Due to technical problems, this schedule was not always adhered to. Therefore, real measurement times were not always the same.

As a last limitation, we shall indicate the technical difficulties associated with the simulator on which the measurements took place since it is not an EASA approved simulator for training purposes and it does not represent an airplane that is used in the modern commercial aviation industry. Because of our limited possibilities, we did not have an opportunity to make these measurements on airline pilots and in an EASA approved airliner simulator. However, we do not believe that this issue would tremendously change the results of our HRV analysis since the subjects are already experienced to fly in real airplanes, therefore, are confident to motion changes in 3 dimensions. So, we assume that there would not be significant differences when the measurements would take place in an EASA approved simulator.

As a recommendation for future studies in this topic, the complexity of the classificators in regression analysis could be improved by adding the indices from the other physiological measurements to the existing model such as EEG data, reaction time, blink rate, pupillary response time. This would enable determination of the most important indices among all physiological parameters. By this way, this work could be a contribution to an even more detailed description of fatigue and could also serve as a support in the future in the introduction of new procedures for physiological testing of pilots.

Despite all regulations and recommendations, it is practically impossible to anticipate and address all possible scenarios that could potentially affect aviation safety as a result of human interaction. Operators, professional pilots as well as general aviation pilots need to be aware of the seriousness of the consequences of fatigue. The basis of theoretical knowledge and knowledge acquired so far should then correspond to the internal functioning of the airline, the behavior of employees, and the safety culture within the employees, especially among pilots.

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