Ennio Idrobo-Ávila was born in Popayán, Colombia in 1989, he has since childhood displayed a strong interest in music. He completed a BSc in Engineering Physics, and a PhD in Engineering. His early research was founded upon his love for music in general and more than 20 years of devotion to the guitar. His parallel interest in such areas as Music therapy, Physiology, Cardiology, Cognitive Neuroscience, and Experimental Psychology led him to focus attention on the effect that musical elements might have on the behaviour of the heart.

Co-authors: **Humberto Loaiza-Correa, Flavio Muñoz-Bolaños, Leon van Noorden, Rubiel Vargas-Cañas.**

To investigate the association between heart activity and sound stimuli, a methodology based on digital signal processing (DSP) and artificial intelligence (AI) was applied in order to examine the effect of musical structures and noise on ECG and HRV. In experiments, it was possible to recognize the valence judgment of participants using binary evaluation and ECG signals. The outcomes revealed a high performance of 0.91 AUC and a similarly high accuracy of 0.86 in recognizing emotional valence, as elicited by instrumental sections of music. Using machine learning, noises and harmonic intervals were found to alter heart activity distinctively: the ratio between the axis of the ellipse fitted in the Poincaré plot was found to change on exposure to harmonic intervals and noise. Moreover, the employed techniques, DSP and AI, were able to demonstrate that the heart reacted differently to different stimuli. For example, the frequency content of the noise and harmonic intervals produced different heart responses and in the case of harmonic intervals, the effect of consonance quality could be detected in the heart response, supporting the theory concerning the biological influence of consonance-dissonance perception. It was observed that different types of noise, harmonic music intervals, and instrumental sections of music generated different patterns in the captured heart signals recognized by the techniques used in the analysis. The results of this research thus represent a valuable contribution to the fields of perception and health.

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Music and the Heart

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Musical structures and the heart;
through the lens of artificial intelligence

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Dedication

I would like to dedicate this study to musicians, scientists, and all those who love music and believe in it, and in its great capability to help human beings and improve the world.

Acknowledgments

I want to give thanks to God, life, and music for allowing me to carry out this research. I am very grateful to Dr Humberto Loaiza-Correa for accepting me in the doctorate program and including me in his PSI research group; thanks too to my research team: Flavio Muñoz-Bolaños for his advice related to the field of physiology; Dr Leon van Noorden for all his interest in this study, efforts and contributions at all stages, especially for his help during my research stage at IPEM; further thanks are due to Dr Juan F. Cardona Londoño for his advice related to the field of psychology, while I am tremendously grateful to my family (Edelmira Avila-Saavedra, Hugo Idrobo-Ramírez, Anyi Idrobo-Ávila, and Sofía Manzano-Idrobo) for all their support and company; to Colin McLachlan for all his help related to the language and document edition and contributions to this research; finally, I would like to offer my fullest gratitude to Dr Rubiel Vargas-Cañas who has believed in me and has made the whole research process possible - he has been there during all the study stages and has been my inspiration in achieving the proposed goals.

Ennio Idrobo-Ávila

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Abbreviations

AI	Artificial intelligence
ANS	Autonomic nervous system
AUC	Area under the ROC curve
BP	Blood pressure
BPM	Beats per minute
CVD	Cardiovascular disease(s)
CWT	Continuous wavelet transform
DBP	Diastolic blood pressure
DSP	Digital signal processing
ECG	Electrocardiography - electrocardiogram
EEG	Electroencephalography - electroencephalogram
EMG	Electromyography - electromyogram
EDA	Electrodermal activity
GAN	Generative adversarial networks
GSR	Galvanic skin response
HCI	Human-computer interaction / Human-computer interface(s)
HF	High-frequency power - HRV
HMI	Harmonic music interval(s)
HR	Heart rate
HRV	Heart rate variability
HT	Hypertension
LF	Low-frequency power - HRV
MCC	Matthews correlation coefficient
MIR	Music information retrieval
NN50	Number of adjacent NN intervals which differ by at least 50 ms - HRV
PPG	Photoplethysmography
RMSSD	Root mean square of successive differences - HRV
SBP	Systolic blood pressure
SDNN	Standard deviation of RR intervals
VLF	Very low-frequency power
WHO	World health organization

Glossary

Artificial intelligence (AI): Artificial intelligence (or machine intelligence) refers to systems that display intelligent behaviour by analysing their environment and taking actions—with some degree of autonomy—to achieve specific goals.

Area under curve (AUC): The area under a curve between two points is calculated by performing the definite integral. In the context of a receiver operating characteristic for a binary classifier, the AUC represents the classifier's accuracy.

Artificial neural network (ANN): Artificial Neural Network, or Neural Network, is a computational model in machine learning, which is inspired by the biological structures and functions of the mammalian brain. Such a model consists of multiple units called artificial neurons which build connections between each other to pass information. The advantage of such a model is that it progressively "learns" the tasks from the given data without specific programming for a single task.

Classification: Classification is a general process for categorization which assigns a label to the samples. A classification system is an approach to accomplish categorization of samples.

Convolutional neural network (CNN): A convolutional neural network is a specific type of artificial neural network that uses perceptrons, a machine learning unit algorithm, for supervised learning, to analyse data. A CNN consists of an input and output layer as well as multiple hidden layers which are formed as mathematical operations. The hidden layers include convolutional layer, pooling layer, normalization, and fully connected layers.

Data: Data is a collection of qualitative and quantitative variables. It contains the information that is represented numerically and needs to be analysed.

Data mining: Data Mining is the process of data analysis and information extraction from large amounts of datasets with machine learning, statistical approaches. and many others.

Deep learning (DL): Deep Learning is a subfield of machine learning concerned with algorithms that are inspired by the human brain that works in a hierarchical way. Deep Learning models, which are mostly based on the (artificial) neural networks, have been applied to different fields, such as speech recognition, computer vision, and natural language processing.

Digital signal processing (DSP): Digital signal processing is the art of using computer technologies to enhance, analyse, or manipulate images, sounds, radar pulses, and other real-world signals.

Electrocardiogram (ECG): ECG is a signal that describes the electrical activity of the heart. The ECG signal is generated by contraction (depolarization) and relaxation (repolarization) of atrial and ventricular muscles of the heart.

Harmonic music interval (HMI): Harmonic music interval is related to two notes played at the same time.

Heart rate (HR): Heart rate is the speed of the heartbeat measured by the number of contractions of the heart per minute (bpm).

Heart rate variability (HRV): Heart rate variability is a measure of the balance between sympathetic and parasympathetic mediators of heart rate.

Label: Also known as annotation. In supervised learning, the answer or result portion of an
example. Each example in a labelled dataset consists of one or more features and a label.

Machine learning: Machine Learning is a field in computer science that builds computational models that have the ability of "learning" from the data and then provide predictions. Depending on whether there is a supervisory signal, machine learning can be divided into three categories: the supervised learning, unsupervised learning, and reinforcement learning.

Random forests (or random decision forests): Random Forests or Random Decision Forests are ensembling learning methods for data classification and regression. They construct a multitude of decision trees during the training and output the class that is the mode of the classes (classification) or mean prediction (regression) of the individual trees.

Supervised learning: Training a model from input data and its corresponding labels. Supervised machine learning is analogous to a student learning a subject by studying a set of questions and their corresponding answers. After mastering the mapping between questions and answers, the student can then provide answers to new questions on the same topic.

Foreword

Rushing water, flapping wings, a pounding heart; whether it's a funky drum loop or a throat singer from a distant land, sounds and music have the power to stir something inside of us. Exactly where inside retains no small element of mystery, but movements of pleasures and sadness, and all senses, noted Aristotle, seem to be beginning … in the heart.

As far back as 1496, in Practica Musicae, composer-theorist Franchinus Gaffurius wrote that the proper measure of the musical beat should be the pulse of a healthy human. Merely to live, enthused the king of pop, Michael Jackson, is to be musical, starting with the blood dancing in the veins; everything living, stated the songster, has a rhythm.

Using the tools of digital signal processing and artificial intelligence, the author herein sets out to dismantle the mystique and to gain at least a useful foothold towards understanding the true rôle that music can play in the field of therapy, with the aim that crotchets and minims might become part of the toolkit of every physician.

This initial work, then, of a talented musician and dedicated researcher has its own sure and exploratory heartbeat, as it goes along, steadily tweaking the questions and seeking out answers, turning, as it were, a scanning microscope on the hidden relationships between musical sequences and measurable heart signals - on profound relationships concealed, we might say, in a twin and in a twang – the twin twang of the Spanish guitar string and the heart string.

Colin McLachlan
Science journalist & editor

Chapter I - Introduction

If we knew what it was we were doing,
it would not be called research,
would it?

Albert Einstein

Introduction

1.1. Cardiovascular diseases and their relevance

Cardiovascular Diseases (CVD) are chronic diseases representing the leading cause of death worldwide [1]. They affect both heart and blood vessels [2] and, in most cases, have a long evolutionary development and few signs and symptoms as the disease progresses [3]. The most common include heart disease, stroke, and hypertension (HT). Furthermore, HT is a cardiovascular risk factor of high prevalence worldwide, characterized by high levels of blood pressure (BP) [3].

According to the World Health Organization (WHO), CVDs caused 17.9 million deaths in the world in 2016 [1], some 31% of total deaths (Figure 1). In Latin America, mortality due to CVD has increased over last decade, causing more deaths than any infectious disease [4], and in 2015 about 35% of the population was diagnosed with hypertension [5].

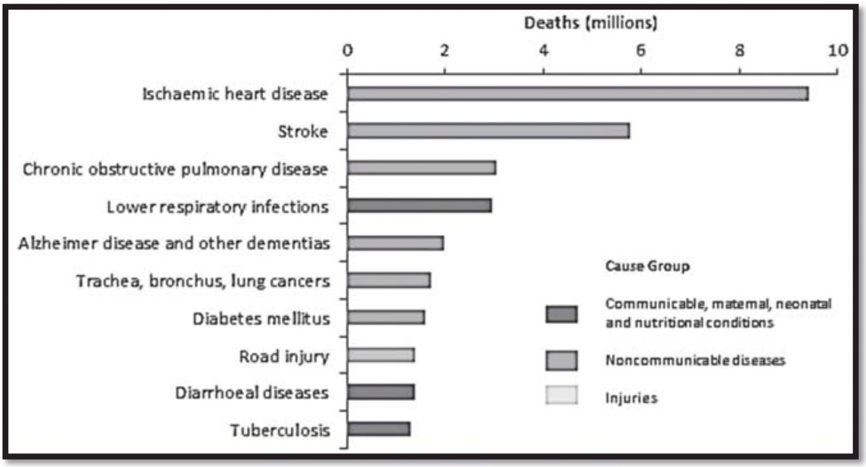

Figure 1. Top ten global causes of deaths, 2016 [6]

As regards HT, according to WHO, in 2008 about 40% of adults older than 25 years had been diagnosed [7]. WHO assumes HT as a public health problem since it affects more than 30% of the world population and is estimated to reach more than 35% of the population in 2025. The numbers around HT are worrisome; the overall prevalence of high BP (equal to or higher than 140/90 mmHg) in adults was around 22% in 2014 (Figure 2) [8].

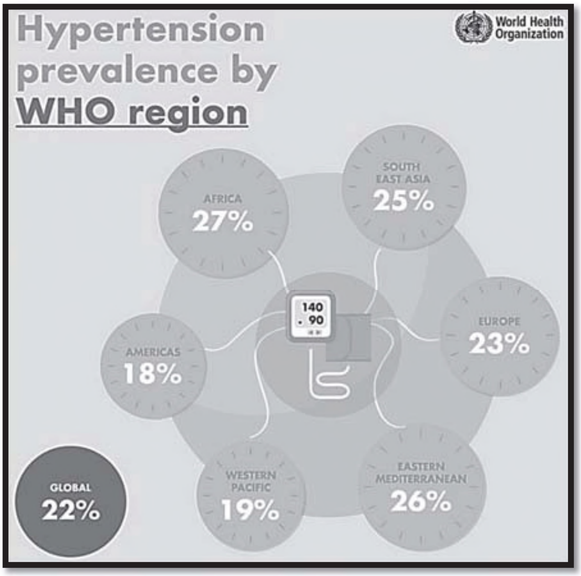

Figure 2. Prevalence of hypertension by WHO region [9]

Two types of interventions are used in treating and controlling CVD, one pharmacological, the other, non-pharmacological. In the case of HT, the pharmacological intervention is related to prescription of medicines; usually, HT medicines belong to one of the following types: angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), beta blockers, calcium channel blockers, and thiazide diuretics. The non-pharmacological intervention is mainly related to lifestyle changes. Suggested life changes may involve weight reduction for the obese or overweight; a reduction in the consumption of sodium (salt), alcohol and tobacco; regular physical activity; and the adoption of a healthy diet [10]. The use of diverse non-pharmacological interventions is generally emphasized to avoid the excessive intake of medicines, in such a way that any associated side effects are diminished.

However, in addition to the more traditional non-pharmacological treatments for CVD, an interesting further option is music therapy [11] [12]. Music is known as a tool that can be used to improve several aspects of health. For instance, the literature shows that music can improve both blood pressure (BP) [13] [14] and heart rate (HR) levels [15]. In many cases, these findings have been associated with mood induction, due to the emotions elicited by music or stimuli [16] [17]; however, previous research does not provide elements for drawing clear conclusions in this matter [18].

Despite good outcomes and trends in previous research, there is still no clear consensus on the mechanisms of influence and the cause-effect relationship between music and the response of the human body [14]. The need therefore remains to determine the magnitude of the effects [19] and why music produces benefits in health [11]. Another aspect still to be clarified is associated with which element or elements of music have more influence over human physiology and psychology and likewise, it would be useful to study what kind of music might produce the greatest effect and estimate what might be the minimum time for a musical sound to produce an effect, or in terms of therapy sessions, the minimum number of sessions to obtain the desired result. As can be observed, many aspects related to music and its effect on humans still remain to be resolved.

The present work is focused on determining whether or not specific elements of music are able to produce changes in heart activity. The focus is placed firmly on harmonic music intervals. These are studied in two different octaves, lower and higher. In addition to harmonic music intervals, a selection of coloured noises is also studied.

1.2. Benefits and importance of research on cardiovascular variables, signal processing and perception

1.2.1. A scientific vision

In recent years it has become necessary to use computing methods and signal processing to extend the human scope related to both the sense of vision and the ability to extract information in the analysis of ECG signals. Information extraction from ECG readings related to the sympathetic or parasympathetic domain under diverse conditions, the association with emotional states, and the influence of sound stimuli is as important today as it is generally ignored. Work ought therefore to continue to make a contribution to the reading of ECG signals from a number of viewpoints.

Digital signal processing aims in the main to enhance the reproducibility and data extraction of ECG signals compared to traditional manual measurement or visual appraisal [20]. In various ECG digital signal processing applications, it is possible to encounter stages in common, such as denoising, feature extraction, classification, and data compression. During the last few decades, in each of these processes new techniques have emerged that improve their performance. There are nevertheless many elements that can be enhanced and challenges which need to be figured out [21].

The literature review, no studies were found that looked for a correlation between stimuli signals and their effect on ECG. As a consequence, there are no specific biomarkers (features) in ECG to correlate these signals with sound stimuli. Meanwhile, trends in artificial intelligence applied to cardiology show that most supervised algorithms are regularized regression, tree-based methods, and support vector machines [22], whereas the most widely used unsupervised algorithms are neural networks and deep learning [22]. Given that deep learning is a rapidly-growing, booming technique and new studies are required with an application in ECG signals, this approach will be used for data analysis. This research will thereby contribute to diverse aspects of the academic field in digital signal processing of ECG signals related to sound stimuli.

The literature review also revealed a genuine need to continue research related to the influence of sound, noise, and music on psychophysiological variables. It is known that noise can affect several aspects of humans, both psychological and physiological. However, the studies from this review do not show a common trend. It is therefore important to consider future research to observe and understand the psychophysiological response to different types of noise, such as traffic noise.

1.2.2. A social vision

In this light, promotion of non-pharmacological elements for CVD management is incentivized, including those of listening to music and music therapy itself. The research that been carried out to date has assessed the effects of music on physiological variables of the cardiovascular system, providing evidence that backs up the likelihood of using music as a support element in the treatment and control of CVD. In addition, prior research has begun to demonstrate how music could be applied for this purpose. Such advances in research on this topic render music therapy a relevant element that will most likely contribute to the well-being of people. With the present research therefore, a quantitative viewpoint seeks to discern whether or not specific musical structures might affect cardiac functioning (ECG signals).

1.2.3. A methodological vision

As regards digital signal processing techniques, a new national vision has opened up looking to generate new research relating music to its effects on diverse physiological variables. It is observed that this is a field of considerable amplitude that may help people around the world from both the academic and social viewpoints. With this research, the aim is to influence academic aspects related to digital signal processing, music, and physiological variables.

Regarding classification techniques, deep learning has been used for several purposes in recent years, mainly in classification tasks. Although a widely used tool, its spectrum of application still requires to be expanded. Accordingly, it is worth noting that in the literature review, the application of deep learning to associate or correlate audio signals with ECG signals was not found as it is proposed in the present research.

1.3. Elements that still require study - Compilation

From the literature review conducted for this research, a number of gaps were found that require further study. These include:

a. The influence mechanisms and cause-effect relationship between music and its effect on the human body [14]; determine the magnitude of the effects [19] and how music produces benefits in health [11].
b. Which element or elements of music have more influence over human physiology and psychology.
c. Of the various dimensions within which music can be analysed (pitch, tempo, rhythm, volume, timbre, texture, duration and form), only pitch, tempo and rhythm have been studied in detail [23].
d. What kind of music might produce the greatest effects; the minimum time for each listening session; the minimum number of these sessions to get the desired or anticipated results.
e. Any correlation between sound stimuli and their effect on ECG; establish specific biomarkers (features) in ECG to correlate ECG signals with sound stimuli.
f. Incorporate more elements of musical analysis to see whether MIR features can allow better discrimination between ECG signals [24].
g. Continue research related to the influence of sound, noise, and music on psychophysiological variables.
h. Consider music with a deeper approach to be able to better figure out how specific elements of music might produce changes in psychophysiological variables [25].
i. Observe and understand the psychophysiological response to different types of noises (coloured-noise: blue, brown, grey, pink, purple, white).
j. What are AI technologies able to reveal about the perception of elementary parts of music, such as harmonic musical intervals.
k. Do periods shorter than ten seconds allow a similar HRV analysis to that traditionally explored using ultra-short ten-second measurements [26] [27].
l. Explore the potential of transfer learning in the analysis of HRV signals.
m. Implement standardised methodologies in high-quality, systematic study in the area of health and perception of the effects of music on the heart, using ECG and HRV [28] [29] [30].
n. Develop new metrics for each specific application [31] [32], for example for applications related to the effects of sounds on ECG and HRV.

o. In the field of human-computer interaction (HCI), determine the extent to which implicit interaction interfaces such as those using physiological measurements (e.g. ECG) enhance human bandwidth in control or interaction [33]
p. While the physiological response elicited by music has been assessed using ECG and HRV signals [34] [35], in general the studies consider a two-dimensional emotion space and do not incorporate each subject's own perception [36].
q. Classification of emotion has generally used music previously classified according to the emotion it is able to produce (emotional music).
r. Even then, such classification rates oscillate between a low 60 to just 90% [37] [38] [39] [40] in the best cases, leaving room for improvement.

1.4. Objective

From an academic viewpoint, this study opens a door to new research at a national level where music and its effects are related to ECG signals. It also seeks the integration of audio signal analysis with biological signal analysis. Not only is health in general strengthened, but a new research field able to integrate several disciplines is thus invigorated.

1.5. Structure of this document

In the present document, the chapters respond to different research objectives, as follows: Chapter I contains the Introduction; Chapter II provides the referential framework; next, the recognition of valence judgments in music perception using electrocardiographic signals and machine learning is presented for musical excerpts in Chapter III and for harmonic music intervals in Chapter IV. Finally, Chapter V lays out the Conclusions, covering a general overview of the research, the main conclusions, suggestions, contributions and achievements. Each chapter is presented as a stand-alone document containing the following sections: Introduction, Methods, Results, Discussion/Conclusion and Bibliography.

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Chapter II – Different types of sounds and their relationship with electrocardiographic signals and the cardiovascular system

Good, sound research projects begin with straightforward, uncomplicated thoughts that are easy to read and understand.

John W. Creswell

Referential framework[1]: Different types of sounds and their relationship with the electrocardiographic signals and the cardiovascular system - Review

2.1. Introduction

Sound is a mechanical vibration which travels through an elastic medium, as a variation in the pressure exerted on the particles which comprise it [1]. Sound can be perceived as pleasant or unpleasant, although the boundary that separates music and noise can be very thin and subjective. Most unpleasant sounds are several noise types, and, despite some elements and preferences, pleasant sounds are frequently related to music [1]. However, the task of differentiating different types of music from noise becomes a question of aesthetics, outside the scope of this document. Normally, noise (e.g. traffic and factory noises) is linked to unpleasant sounds, nonetheless sometimes it is not directly associated with them (white noise or background noise, i.e. ambient sound) [2]. On the other hand, music is associated with pleasant sounds (frequently music types as classical, relaxing or sedative) although they are conditioned by preferences and familiarity [2] or the listener´s cultural association [3]. Regarding sound effects, research has shown sound produces effects on human health, in both physically and psychologically [4]. However, the effects on human health have not been fully understood and explained, or how sound may contribute to improve human beings quality of life.

As sound may generate both positive and negative effects on humans, [4], it may also contribute to the treatment of some diseases. It can also be a control instrument in such cases. Therefore, it is worth studying the relationship and effects of sound on human health [5] and to address this topic in order to understand whether those effects are related to pleasant and unpleasant sounds [2], or if they respond to specific structures of the sound. In general, previous work has shown that negative effects could be related to exposure to unpleasant sounds, such as noise [6]. Whereas in many cases, the positive effects could be related to interaction or to listening to pleasant sounds, such as music [7,8].

Understanding these relationships, may make it possible to achieve benefits in several areas. Thus, in health it may be possible to prevent or reduce harmful effects in which may be produced by exposure to harmful noises. Additionally, it may be possible to improve the use of music therapy in

[1] This section is a part of the published article by Ennio Idrobo-Ávila [31]

several physiological and psychological conditions such as hypertension, cardiovascular disease [9], migraine, headaches, gastrointestinal ulcers, autism, dementia, depression, pain and stress management, mental disorders [10]. Another important element of considerable interest currently, is the relationship between the brain and the heart. Sound and music research may provide relevant tools to contribute to this topic, since music is a stimulus which can affects the whole brain and promotes interaction between its hemispheres. Improvements in health also have economic benefits, specifically in the health sector, since it is probable that application of sounds and music may able to reduce consumption of some medicines. Similarly, in the IT sector, topics related to emotions and relationships between people and machines may be improved where music could be a way to study them. Also, understanding the relationship between sound and humans and knowing the mechanisms related to how sound affects the human body, could improve and promote new applications in emergent technologies, such as, the Internet of things and virtual reality.

Some types of sound, such as noise, can also produce harmful effects whereas other types of sound, particularly music, can contribute to improving physiological and psychological health. However, it is not completely clear yet what the effects or the mechanisms of musical sounds are on the human body. Thus, it has been observed that exposure to noise increases blood pressure and heart rate [11–21], whereas music evokes emotions and has effects on mood, memory, stress levels and anxiety. The effects of noise have also been seen on several of the body's systems, such as nervous, cardiovascular, respiratory and endocrine, where it can influence physiological variables, such as respiration, heart rate, blood pressure and many more. [5].

Since the early twentieth century, the effects produced by sounds, such as music have been registered using measurement equipment [22]. Current technology can now be used to register the effects produced by different sound stimulus in more detail to moves towards a clearer understanding of how the human body is affected by them. Considering the positive and negative effects of sounds on human health, it is important to carry out new research to reduce the negative effects and understand the ways in which we can take advantage of the positive effects.

Nevertheless, previous research has gaps which need to be addressed. One of the most important is related to the size of the sample. In many cases, the sample is very small and the conclusions do not allow us to make generalizations. However, as in much medical research, this problem has a complex solution. It is difficult to find a sample with all the necessary elements under control and wide homogeneity, such as, age, current diseases, gender, education level, conditions and lifestyle.

Other difficulties are related to experimental design, specifically the control group. A lot of research has used a control group in silence, but in these situations the effects obtained in all groups could be not compared since the control group does not have an auditory stimulus. [5]. On the other hand, most of the previous reviews related to this topic have included very few studies, so it is difficult to have a wide view their common and uncommon results, and a general vision of their advances and gaps.

Focusing on this review, sound can be classified in different ways according to its characteristics. However, for this paper it is important to differentiate between sounds that are pleasing to the ear, including music, and noise. In general, although music and noise are mixtures of different frequencies, pleasant sounds and music can be distinguished from noise. In the case of music, there is a certain order, its frequencies are discrete (separable) and rational (their relationships from simple fractions) with a discernible dominant frequency. This can be described mathematically by an infinite sum of sines and cosines multiplied by appropriate coefficients. On the other hand, noise has no set order. Its frequencies are continuous (each frequency will be present in some range) and random (described by a probability distribution) with no discernible dominant frequency.

In this paper, a systematic review is conducted in order to integrate research related to several sound types both pleasant and unpleasant, specifically noise and music. In this review, infrasound and ultrasound were not considered. Moreover, this paper seeks to include as much research as possible to create a more general vision about relevant elements regarding methodologies, study subjects, stimulus, analysis and experimental designs in general. By doing so, it will be possible to find common elements and gaps in research between studies; common responses between different stimulus. Therefore, this review explores sound as a general element of particular aspects like noise and music types and their effects on physiological and psychological variables.

This approach differs from previous ones because here the stimuli are considered as a sound or auditory entity. In other studies, the effects of particular stimuli, such as noise or music is only included. However, it is important to have a wide panorama in which it is possible to find common and different aspects among the outcomes and applied stimulus. Hence, this approach could contribute to the development of methodologies of future research related to the effects of sound on the human body.

Rationale

Nowadays, there has been an increase in research to understand the influence of sound, noise, and music on the human body, and in this case, electrocardiographic signals on the cardiovascular system. There is also a trend to study interaction between humans and the machine, where understanding, processing and classifying emotions play an important role. In this case, music is a relevant tool because it can evoke emotions and memories through auditory memory. Thus, it is necessary to understand how music influences human physiology and psychology.

Objectives

The aim in this review is to understand previous research in this topic, in such a way that the main findings will be highlighted and research gaps and important issues will also be found to be considered in new studies related to this topic.

Research question

This review intends to answer the questions below:

How sound, noise and music influence electrocardiographic signals and the cardiovascular system?

Four secondary questions were formulated related to the sample, the sound types, the listening sessions, and the tools for analysis:

1. Which characteristics related to gender, age, health condition, and size have the samples considered in the selected studies?
2. What types of sounds have been used most frequently?
3. What characteristics do the listening sessions have in the selected studies?
4. What mathematical, processing, and analysis tools have been used to analyze the results?

2.2. Methods

This section describes the review methodology. Thus, details of participants, interventions, and comparators are shown. In addition, it explains, the review protocol, search strategy and register, inclusion and exclusion criteria. It also lists the data sources, studies sections and data extraction.

Participants, interventions, comparators

The search, assessment and selection of documents were performed independently by four research groups from different universities. In this case, researchers belonging to IPEM Institute for Systematic Musicology - Ghent University, SIDICO and SIFIEX - Universidad del Cauca, and PSI - Universidad del Valle participated in this review. Within each group there were one or more researchers who participated in search, selection, evaluation or analysis of documents independently. At the end of the review, a comparison was made between results obtained by each one of the researchers. Decisions were made about non-concordant results (such as inclusion and exclusion criteria and paper selection) between the research groups. The information was then extracted and synthesized to respond to the formulated research questions. Finally, the results, analysis and conclusions were organized in a document for the drafting of this article.

Systematic review protocol

The systematic review in this paper followed some sequential steps so that they can be reproduced in further research. First, searches about the topic were made in different databases and carried out following the same procedures to establish the same search conditions. Thus, the same filters and inclusion-exclusion criteria were used. Second, classification by categories of searched documents was made to find an answer to the research question raised. At this point, a reading of these documents was done and those which did not satisfy all inclusion criteria were discarded. Next, the documents collected by each group of researchers were collected together in a unique database and duplicates were removed. Finally, the selected documents were read and analyzed independently by each group of researchers and subsequently conclusions were established between them. In this way, the proposed review protocol allows carrying out a more complete search with less risk of bias and which can be reproduced in several contexts.

Search strategy

The search strategy was made through an initial selection of keywords and construction of three different search equations. In order to search the documents, the following keywords were used: ECG, EKG, electrocardiogram, electrocardiography, electrocardiograph, sound, noise, and music. With keywords, they were constructed 3 search equations, which are referenced as SE1, SE2, and SE3:

SE1. TITLE-ABS-KEY (sound* AND (electrocardiogra* OR ecg OR ekg))

SE2. TITLE-ABS-KEY (music* AND (electrocardiogra* OR ecg OR ekg))

SE3. TITLE-ABS-KEY (nois* AND (electrocardiogra* OR ecg OR ekg))

In these cases, an asterisk (*) was used as a wildcard element; for instance, "electrocardiogra*" includes results relate to electrocardiogram, electrocardiography or electrocardiograph. Furthermore, logical operators were used, such as AND to restrict and OR to extend the search. This way, with these keywords, logical operators and search equations, documents were searched using selected databases.

Search register

Search register was made individually in each research group and in the final stage an average was taken with the registers. Initially a unique search in Scopus with first search equation was made and 3457 documents published between 1912 and 2017 were found. In this search it was noted that the first big peak in publications happened in the 1970s, when there was an increase in research into this topic. However, most of the research into this area was published between 1999 and 2017, with a peak in 2015. This paper focuses on only the most recent studies, between 1999 and 2017. Thus, documents published before 1999 were filtered. The amount of papers per year in Scopus related to sound and music are graphed in Figure 1.

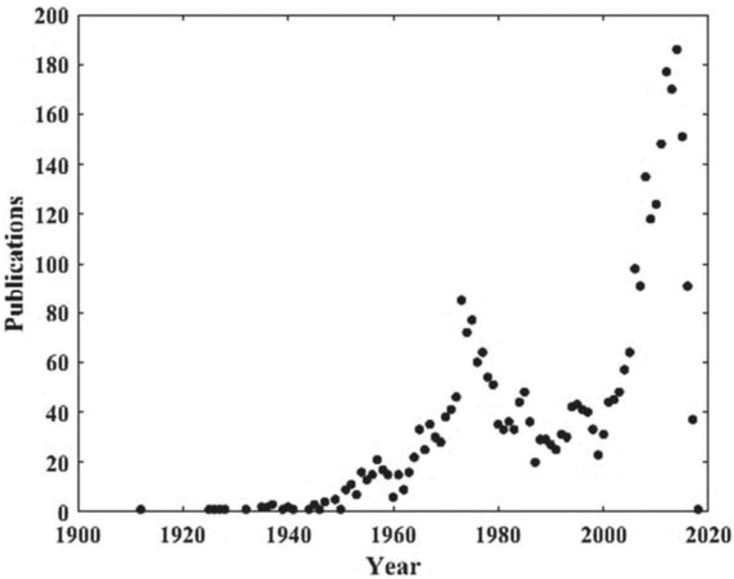

Figure 1. Amount of papers per year in Scopus and related to sound and music

Inclusion criteria

In this review, the inclusion criteria relates to: document types, language, year of publication. Stimuli and variables of interest were considered. Thus, document types included were those produced as original and review papers written in English, Spanish, or Portuguese and published between 1999 and 2017. Additionally, the human population according to the exclusion criteria and studies related to the influence of listening to sound on electrocardiographic signals or variables of cardiovascular system were considered uniquely. Moreover, documents relating to heart rate and heart rate variability were included. There is a particular interest in research with an experimental design which includes sound reproduction. In these types of studies, subjects hear an acoustic or auditory stimulus and their effects on electrocardiographic signals or the cardiovascular system are studied.

Exclusion criteria

As in inclusion criteria, document types, population sample, stimuli and experimental design were considered. Documents with opinions, points of view or anecdotes were discarded. In addition, studies with subjects younger than 18 years, children, newborns, and fetuses were discarded. Also, research with study subjects in a state of depression or with pathologies such as dementia, cognitive disability, disorders of consciousness, cerebrovascular disease, and vegetative state were discarded. In the same way, studies in which visual stimuli were presented were discarded. Therefore, research which presented stimuli with video or moving images were discarded. Studies which considered active music therapy where subjects make music in any way were excluded. This way, with these exclusion criteria, researchers excluded research which deviated from the analysis and the conclusions related to the main topic and research question.

Data sources, studies sections and data extraction

To answer the proposed questions, a search in several scientific literature databases was made. A search was carried out in databases relating to engineering, medicine and psychology. Databases like IEEE, PubMed, and Frontiers were consulted. Moreover, Scopus as a general database was consulted. By searching databases from different disciplines allowed us to have different viewpoints and perspectives.

2.3. Results

After presenting the methods to carry out this review, the obtained results are shown. The selected studies in this review present some characteristics with significant variability. Thus, the observed effects, the most common elements and some differences between research are presented. First, characteristics of samples used in the selected studies are shown. Then, a section about different stimuli provided in included research is presented. Once the presentation has occurred, the results relating to stimuli show the listening sessions´ characteristics. After this, mathematical, processing and analysis tools often used in selected research are revealed. Lastly, the more common measured variables in this review are presented.

Flow diagram of the studies retrieved for the review

Figure 2 shows the flow diagram of the studies retrieved for the review from the selected databases with number of documents.

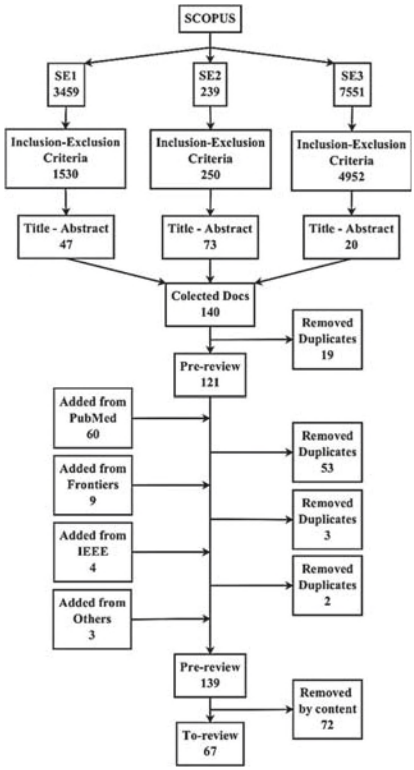

Figure 2. Flow diagram of the studies retrieved for the review

Effects of stimuli

Selected research in this review has provided some effects with slight trends between them. Changes observed in measured variables as a result of presented stimuli are shown in Figure 3. In this case, general and significant changes in some variables as a product of exposure to stimuli are noted. However, most of these changes did not present a trend in most cases, with the exception of noise studies where both BP [11,15,18,20,23,24] and HR [11,13,14,18–21] increase or tended to increase. Additionally, an increased risk of Myocardial Infarction was noted (MI) as levels of noise intensity increased [25].

Another element to note is related to changes in common variables between different stimulus. Heart Rate Variability - HRV (HF and LF/HF) changes with both sound [26–29] and noise [14,16,17,20,30,31] stimuli, whereas GSR changes with sound [32,33] and musical [34–36] stimuli. Moreover, LF also showed changes with exposure to noise [14,16,17,30,31,37]. Here, it is important to note that both sound and musical stimuli can affect memory and emotions. Perhaps they are related to GSR and HRV, particularly HF, which has been linked with the Parasympathetic Nervous System, whereas noise can affect both stress and anxiety levels, they are possibly related with BP and HR.

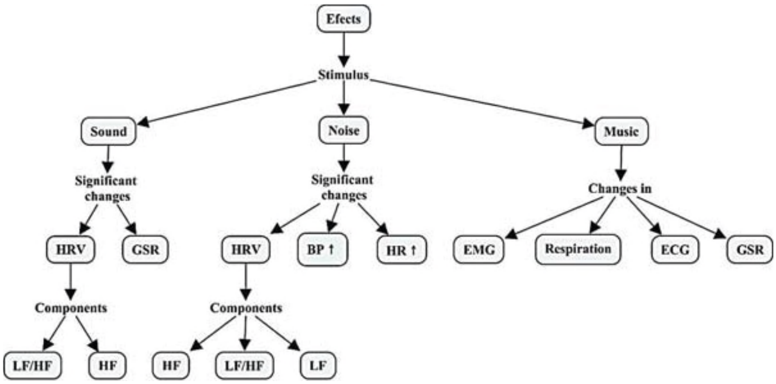

Figure 3. Changes observed in measured variables as a result of presented stimuli
(* Abbreviations)

Sample characteristics

In this review, the selected research presents a great diversity of samples. Most frequently characteristics in used samples are shown in Figure 4. It is possible to see that most selected studies used a sample with healthy subjects [15–18,23,26–29,32,38–48]. Samples are also used with a combination of males and females [12,14,16,17,27,32,33,39,42–44,49]. There were few studies with just males [24,31,37,50] or just females [45,51–53]. With respect to the sample size, many of the studies used a size between 20 to 33 [12,18,19,26,27,32,37,38,43,46,47,51,53–57] or 35 to 88 [15,16,20,21,23,24,29,36,42,44,48–50,52,58–61] subjects. There were few studies with a sample larger than 100 subjects [11,13,14,40,57,62,63]. Similarly, most of the research considered subjects between 18 and 41 [12,13,17,19,26,28–30,36–39,44,49,52,59,62], and a few studies used subjects older than 42 [18,50] as part of the sample.

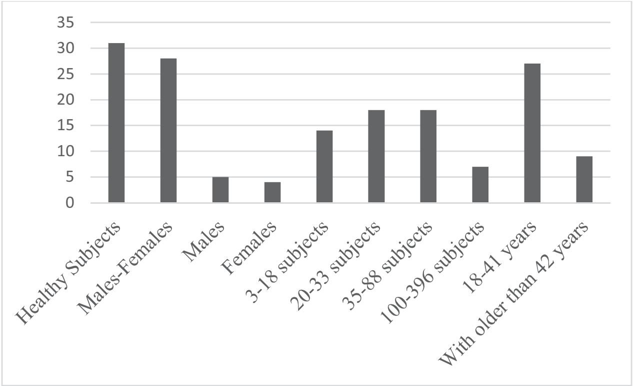

Figure 4. Most frequently characteristics in used samples

Type of sounds, noise and music

As well as sample characteristics, the studies considered have different types of sound stimuli. Thus, most used stimuli in selected research according to categories of Sound (S), Noise (N), and Music (M) shown in Figure 5. There, it is noted that both pleasant [26,32,39] and unpleasant [26,32,39] sound were the most used stimuli in sound research; traffic [15,20,21,58,62], white [12,17,18,40], factory [11,13,23,24], background [15,16,18,41] and low-frequency [31,41,64] noises were used with more frequency in noise studies. Whereas classical [43,45,47,51,54,57,59,60,65] and relaxing or sedative music [46,47,55,63] were most used in music research. It is important to observe that classical music was the most used stimulus. Some studies considered music selected by study subject and in many cases, specifications about the music used was not given.

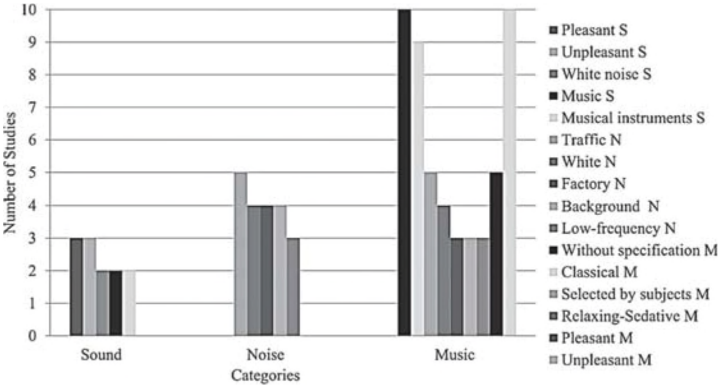

Figure 5. Most used stimulus in selected research according to categories of Sound (S), Noise (N), and Music (M)

Listening session characteristics

In the same way as stimuli and sample, the listening sessions present a wide diversity due to the nature of the research. Most frequently characteristics in the listening sessions are shown in Figure 6. In most of cases it is not considered a control group [11,17,18,26,27,32,34,35,37,39,42,66], just few studies had a control group [15,23,24,50,51,62,63]. In much of the research, stimuli were presented through headphones [12,17,18,26,28–30,32,35,36,39,40,43,55,67]. It is interesting to note that some studies asked subjects to close their eyes [26,27,36,43,55,67] to concentrate on presented stimulus. A seated position was also used [12,15,17,26,28,29,32,37,43,45,47,55] more frequently with respect to a supine position [18,36,44,53,61]. Moreover, in some cases, some environmental elements were controlled [12,15,23,26,27,29,43,55,67]. Another element to note is related to the length of the listening sessions. Many studies had a listening time between 15 and 30 minutes [26,36,38,40,44,54,63,67,68]. Others lasted between 2 and 15 minutes [35,45–47,52,53,56,61]. Only a few listenings lasted between 30 and 60 minutes [27,33,37,50,60], or more than 60 minutes [11,12,31,51].

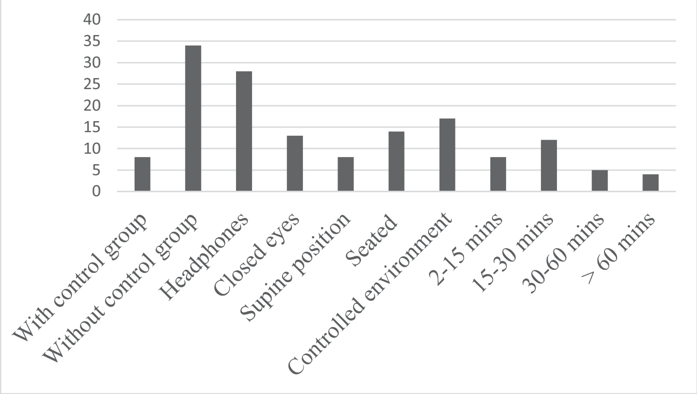

Figure 6. Most frequently characteristics in the listening sessions

Mathematical, processing, and analysis tools

In the selected studies for this review, diverse mathematical, processing and analysis tools were used. The most frequently used analysis tools in the selected studies are shown in Figure 7. There, common statistical tools are observed as mean [20,23,24,31,42,43,63,66] and standard deviation [11,23,24,31,42,43,56,66], which are used frequently; moreover, the most frequent used elements are considered to compare between groups, such as ANOVA [12,17,29,32,34,37,39,43,69] and t-test [11,18,23,33,42,51,61]. Tools with less frequently used, such as Mann-Whitney U test [15,17,41,49,63], Chi-square test [15,23,63], Linear regression [15,23], and classification elements as k-Nearest Neighbors (kNN) [34,35,66,69] and Multilayer Perceptron (MLP) [34,35,55,69].

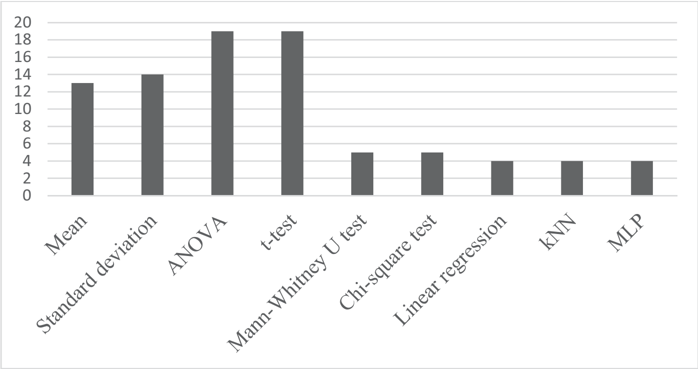

Figure 7. Analysis tools used with most frequency in the selected researches

Measured variables

In this review, studies were selected which researched the effects of music on several physiological variables, especially those related to the cardiovascular system, and psychological variables. The most used physiological and psychological variables in selected researches as shown in Figure 8. According to search criteria, it is noted that most studies measured the ECG signal [11,12,16,23,26,27,29,34,35,39,42,49] In the same way, in many cases the variables derived from ECG as HR [14,17,23,27,32,35–39,44,51] and HRV were selected [12,14–16,26,28,33,35,42,49,66]. In addition, other physiological variables, such as BP [11,23,38,45,52] and respiration [21,34,35,58] were contemplated, as well as GSR [32–35], audiometry [12,23] and EMG [32,34,35] with less frequency. On the other hand, the most used psychological variables were valence and arousal [26,32,39,57,59]. Here it is important to note how psychological variables were measured with less frequency than physiological variables. Thus, it is important to consider the psychological elements in future research.

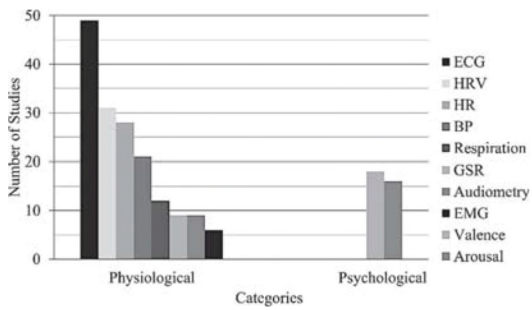

Figure 8. Most used physiological and psychological variables in the selected researches (* Abbreviations)

2.4. Discussion

Summary of main findings

In this section, the main findings according to physiological and psychological responses and its stimuli are presented. It is important to observe that the psychological elements are used in a reduced way respect to physiological variables.

Sample characteristics

In studies related to sound, most of them considered normal or healthy subjects [26–29,32,38,39]; with respect to the sample size, most studies had a sample between 10 and 27 subjects [26–28,33] and others between 30 and 52 subjects [29,32,38]. Most research considered a sample with a mix of males and females [27,32,33,39], and the subjects aged between 18 and 35 [26,28,29,38,39]. Here, most of the studies did not have a control group [26–29,32,33,38,39].

In research related to noise, most considered normal or healthy subjects [15–19,21,23,31,37,40,41,62,64], and others with Hypertension [16,18,23]. The sample size varied widely among the studies. There were studies with samples between 10 and 25 subjects [12,17–19,30,31,37,41,64], between 36 and 88 subjects [15,16,20,21,23,24,58], and between 100 and 396 subjects. [11,13,14,40,62]. Most of the studies used a mix of males and females [12,14,16–19,21,30,40,58,62] and other studies considered only males [24,31,37]. The age variable in the sample was wide, with subjects from 18 to 46 years [12,13,17–19,30,37,62], and studies with subjects with broader age ranges, between 18-62 years [58], 19-50 years [21], 17-41 years [40], 34-74 years [16]. In these studies, some had a control group [13,15,23,24,62] but most did not. [11,17–20,30,37,40].

In research related to music, most studies used a sample with normal or healthy subjects [42–48,50,52,53,65]. Moreover, some studies considered subjects with several health conditions [48,50–52,60]. It is important to note that some studies did not provide a subject specification. [34,57,66,69]. With respect to sample size, it was noted that the sample size varies between 3 to 18 subjects [35,45,57,65,67,68], 20 to 28 subjects [43,47,53–57], 30 to 44 subjects [36,44,46,51,52,57,59], and 60 to 125 subjects [42,48–50,57,60,61,63]. Moreover, most research has had a sample with age ranges between 18 and 41 years [35,36,43–46,49,52–54,59,61,67,68], and other studies had a broader age range, 31-74 years [50,65], 18-65 years [63], 20-57 years [56]. Many studies also considered a sample with males and females [36,42–44,48,49,54–56,59,61,65,67], and others with just males [50] or females [45,51–53]. In these cases, most research did not have a control group [34–36,42–45,49,52–55,59,65–69] and only a few considered a control group [50,51,63].

Most studies considered samples with healthy subjects. Therefore, it is interesting to determine whether healthy subjects respond to sound stimuli in different ways to people with health problems and to investigate how health issues can interfere with reactions to sound stimuli. A lack of control group was also noted in most research, probably due to samples with few subjects which could obstruct both data analysis and conclusion extraction related to stimuli effects. Another point to note is that a lot of research had a sample made up of males and females. Therefore, it will be interesting to establish if males and females are affected by sound stimuli in different ways. If that is the case, it should be taken into account in future research. In studies related with music, it is noted in some studies there was a sample with a wide age range. In such cases, we can consider how the musical perception, appreciation and hence the registered effects of different people might be affected by their generations' tastes. [70]. Thus, sample is an important restriction in experimental design for researches in the health area. A sample could present limitations both in its size as in its characteristics, as age, gender, among others.

Type of sounds, noise and music

In studies with sounds, it has been observed that most studies used pleasant [26,32,39] and unpleasant sounds [26,32,39], as well as white noise [27,39]; however, other sounds, such as neutral [32], pure tone [39], daily life sounds [27], wasp buzzing [28], engine sound [28], drum sound [29], Tibetan singing bowls [33], and some types of music, such as classical and house music have been applied [28]. In studies with noise, most studies took into account traffic noise [15,20,21,58,62], background noise [15,16,18,41], white noise [12,17,18,40], factory noise [11,13,23,24], and low-frequency noise [31,41,64]. Additionally, noises such as impulsive noise [18,40], train noise [19,20], and various noise intensities [41,64], were applied among others. [14,15,30,31,37,40]. In research related to music, most studies used classical music [43,45,47,51,54,57,59,60,65], relaxing or sedative music [46,47,55,63], emotional music [36,44,67], pleasant music [42,48,49], unpleasant music

[42,48,49]; also, new age music and Persian music were taken into account [43,47,51,53], among other kinds of music or stimulus [42,46–49,51,52,56,57,60,61,65,68]. It is important to note that many studies used music selected by study subjects [34,35,47,52,69], and other studies did not give enough information about the music used [34–36,42,44,52,55,63,66,67].

In studies related to sound and noise, it was noted that there was a considerable variety in the stimuli. In these cases, the use of daily life sounds and noises is highlighted since it is possible be aware of their positive or negative consequences on humans. Regarding research carried out with music, it is important to note how several types of music have been used, including music selected by study subjects. It is worth mentioning, that in studies with little information about the music used it is hard to associate it with the registered effects. At this point, this paper encourages future research to promote the use of artificial and electronic music, where possible to control its components efficiently. That way, conclusions regarding the produced effects could provide more information and increase confidence levels. Hence, stimuli used in the selected studies present a great variety stimulus providing a general vision about its effects on the study subjects.

Listening session characteristics

In studies associated with sound, most of them used headphones [26,28,29,32,39], in other studies, subjects were seated [26,28,29,32], and some research controlled some environmental elements [26,27,29]. Moreover, listening sessions lasted between 20 and 60 minutes [26,27,33,38].

In studies with noise, most used headphones [12,17,18,30,40] and others used loudspeakers [19,20,31]. In some studies, subjects were seated [12,15,17,20,37]. Many studies had a control for environmental elements [12,15,19,20,23,24,31]. With respect to the length of the listening sessions, most of researches had a period between 20 and 100 minutes [20,31,37,40,41,64].

In studies related to music, most of them used headphones [35,36,43–46,48,50–52,54,55,59–61,63,65,67]. Here, it is important to note that some studies did not provide information about stimulus presentation [34,53,57,66,68,69]. With respect to the stimulus volume, in some cases the amplifier volume was controlled by the subject [43,44,51,53,67] whereas in other cases, it was fixed or controlled by the research members [46,47,49,56,65]. With regard to the subjects position, in many cases subjects were in supine position [36,44,46,48,53,54,61] but in other cases were seated [43,45,47,50,55]. One element to note is that, in many studies, subjects had their eyes closed [36,43,44,46,48–50,53,55,61,67]. Also, some studies controlled the environmental elements [36,43–46,55,67]. In many cases, the listening period was between 3 and 13 minutes [35,45–47,52,53,56,61], also, in other cases, this period was longer, between 20 and 60 minutes [36,44,50,54,60,63,67,68].

In this section, it was noted that most studies used headphones to present stimuli. This is a good method since headphones reduced the perception of external stimuli which could negatively affect research outcomes. Additionally, through the use of headphones, the stimuli are presented in a more intimate way. With respect to the position of study subjects, it is critical that their position allows them to concentrate or focus in the listening of the stimuli comfortably. Thus, the seated position and the supine position used in many music studies, is ideal. So, where possible it is also important to control environmental elements in the experiment room in such a way that it does not distract people in the study, as happened in some selected studies. It is important to note that in some studies with music, subjects had their eyes closed, eliminating the effects of visual stimuli. This is a valuable element to replicate in future studies related to sound stimuli. Finally, it is noted that most of the selected studies had a minimum listening time session of 20 minutes. This is a crucial factor which requires critical assessment and discussion between specialists in the health area to determine the minimum listening session time to guarantee the presence of the effects produced by sound stimuli.

Mathematical, processing and analysis tools

Regarding studies with sound, it was noted that ANOVA [29,32,39] and the Wilcoxon signed-rank test [26,29,33] were the most used statistics tools. In studies related to noise, the most used analysis tools were ANOVA [12,17–21,37,41,64], T-test [11,18,19,23,24,62], Chi-square test [15,23,24,62], linear regression [15,23,58,62], Mann-Whitney U test [15,17,41], and common statistical elements, such as, mean [20,23,24,31] and standard deviation [11,23,24,31]. In research relating to music, several statistical tools were taken into account, among them ANOVA [34,43,47,48,59,60,69], T-test [42,50–52,61,63] and Paired t-test [46,56,60,61], Shapiro–Wilk statistic [45,48,63], and common elements in statistics, such as, mean [42,43,46,47,50,54,60,63,66] and Standard deviation [42,43,46,47,50,54,56,60,63,66]. Moreover, some elements of machine learning and digital signal processing, were employed, including; k-Nearest Neighbors [34,35,66,69], Multilayer Perceptron [34,35,55,69] and Support Vector Machine [43,44,53].

Most of the studies presented in this section used ANOVA to analyse data along with some classic statistical tools such as T-test. However, in studies with music other analysis elements, such as, machine learning and digital signal processing were used. This trend in the use of analysis tools is in great part due to the fact that many studies in health are developed using classic statistics. This paper encourages the application of new data analysis techniques in future research relating to sound stimuli and its effects, such as, as machine/statistical learning and data mining.

Measured variables

With regard to measured variables, because this review was focused on ECG signals, most studies considered ECG signals and some derived variables as HR and HRV. Thus, ECG was measured in studies with sound [26,27,29,39], noise [11–13,16,17,19–21,23,24,30,31,37,40,41,58,62,64] and music [34–36,42–49,51–57,59,61,63,65–69]. In the same way, HR was present in research with sound [27,32,33,38,39], noise [13,14,17–19,21,23,31,37], and music [35,36,44–46,48,50–52,54,59,60,63,65]. It also occurred with HRV in research in sound [26–29,33], noise [12,14–17,20,30,31,37,41,64], and music [35,42–45,47–49,54,56,63,65,66,68]. In these cases, it is can be seen that ECG is the measured variable, which has a broader frequency in most research.

Respiration was another variable measured in a lot of research. This variable was measured both in studies with noise [13,19,21,58], such as music [34,35,57,59,65,66,69]. Although, respiration was observed in much research it was not as frequent as ECG or its derived variables.

In addition to respiration and ECG variables, other elements were considered for measuring or observation. Thus, in studies relating to noise the variables BP [11,13,15,17,18,20,23,24,31,41,64], Electrooculography [18,19,40] were used. Moreover, it is important to note that some research used audiometry [12,17,19,20,23,24,37,41,64]. Additionally, in studies with music the measured variables, such as, GSR [34–36,48,66,67,69], EMG [34,35,57,66,69], BP [45,51,52,54,60], were used.

Most studies took into account the measurement of physiological variables as well as some psychological elements, such as valence and arousal. Thus, valence [26,34–36,42,43,48,49,55,57,59,66,67,69,71] and arousal [26,34–36,43,48,55,57,59,66,67,69,71] were measured in studies with music. These variables also were measured in studies with sound [26,32,39]. In this way, these studies reveal that both valence and arousal represent important variables relating to human psychology.

In this point, it is important to note that many studies where HRV was considered, used some elements relating to digital signal processing, due to the natural analysis of this signal. Thus, in many cases elements such as Fourier or Wavelet transform, power spectrum, linear and frequency analysis are used. Finally, with respect to ECG acquisition, in most cases where the ECG signal was used, it was acquired from a device with 3 electrodes [13,18,19,21,26,30,32,36,40,44,53,55,58,65,67].

Physiological variables

In studies related to sound, it is noteworthy that there are just a small number of studies, but they vary significantly. In these cases, they considered different sound stimuli and produced responses which differ from each other. As a result, it is a difficult task to find both common outcomes and relationships between effects and observed variables. However, some common elements related to HRV were observed. Thus, it should be emphasized that both HF [26–28] and LF/HF ratio [28,29] were shown as indicators for different stimuli. In addition, it was noted that GSR [32,33] represents an element which presents variation against diverse sound stimuli. Here, a lack of clarity regarding influence of auditory stimuli on HR is noted. Hence, in studies relating to sound, it is evidenced that both HRV and GSR present variations influenced by sound stimuli, but HR is an element on which further research is worth being carried out.

From studies reviewed on the influence of noise, the results found do not establish a trend. Nevertheless, in this case there are some repetitive elements between some studies. Thus, it is can be seen that BP (SBP or DBP) increases or tends to increase [11,13,15,18,20,23,24]. This behaviour is also evident in HR [11,13,14,18–21]. Other elements that have shown changes regarding noise exposure are HF, LF, and LF/HF ratio. Nonetheless, in HF and LF there is no marked trend between studies. Thus, the LF/HF ratio has shown an increase [14,16,17] compared to noise exposure. On the other hand, in HF there was both an increase [16,17,30,37] and a decrease [14,20,31] with exposure to noise. This same behavior is seen in LF, where [16,17] a decrease is shown. [30,31,37]. Thus, these studies demonstrate that both BP and HR are affected by noise, but outcomes related with HRV elements are not clear. Despite these findings regarding noise and its effects, it is necessary to expand research about the psychophysiological response of the stress produced by noise.

Regarding research related to music, studies classifying emotions evoked by listening to music, show further evidence of a relationship between emotions, music, and some physiological variables. For classification, the physiological variables which were considered with more frequency were ECG signal [34–36,43,55,61,66,67,69] and GSR [34–36,66,67,69], as well as EMG and respiration [34,35,66,69], in addition to others which were used with a lesser extent. Consequently, these variables are linked very much with emotions in general as well as listening to music.

In addition to ECG, GSR, EMG and respiration, it should be noted that the studies observed do not allow us to establish accurately if music is an influence on HR or HRV. Therefore, it was noted that HR presented an increase [48,59] and also a reduction [54,65] in different research. In this case, it is difficult to draw a conclusion on this point since stimuli between the studies had different characteristics. This is therefore another element to be developed in future research.

Besides electrocardiography (the most frequently acquired signal), there were other registers, such as, respiration and blood pressure. Therefore, it is important to consider, ECG signals and other variables related directly with the cardiovascular system, as well as others which are not, such as, GSR. All registers may support or to contribute to findings in the variable of interest. Thus, with more registers covering the entire cardiovascular system, there will be a greater possibility of finding a relationship between cause and effect in a particular variable, such as, ECG in this particular case.

Psychological variables

As well as physiological variables, it is important to know how psychological variables are affected by auditory stimuli. In this review, it was noted that valence and arousal were the psychological variables used the most to model emotional states evoked by sounds and music. However, they were not considered in studies with noise. In addition to these variables, other elements such as personality and anxiety were considered to a lesser extent. Thus, although psychological elements have an important role in auditory perception, they had been not included in research in a rigorous way.

Valence or arousal dimensions were used to classify emotions [26,34–36,43,55,66,67,71]. Some studies showed which emotion differentiation was easier in arousal than valence dimension. [34,66]. Another aspect to note, was that pain perception can be affected by musical tempo through the arousal of the listener. Pain ratings were highest for fastest tempos [59]. Thus, emotions may be represented throughout valence and arousal. Moreover, music tempo might influence the perception of pain.

With respect to personality, emotions and physiological response to auditory stimuli, [32] it was observed that the personality trait anxiety had an influence in response to affective stimuli, whereas in [39] interaction of affective valence sounds with cardiac response was observed. In the same way, in this case [42] a correlation between emotional personality and ECG amplitude was found. In addition to ECG, [55] EEG signals were registered where both ECG and EEG changed emotional valence from negative to positive after listening to Quranic recitation. However, relaxing music changed arousal state and valence in EEG in a positive way. Whereas, relaxing music produced a negative change in the ECG signal. As a result, these studies show an influence of auditory stimuli on cardiac function, where in some cases, an ECG signal was registered throughout. Elements, such as emotions and personality, may also affect the ECG signal. In this sense, there could be evidence of a relationship between the brain and the heart.

Finally, it is important to note that [35] the arousal change was related to GSR and EMG, whereas valence was linked to ECG and respiration. On the other hand, in [48] it was found that the emotional valence of music affects ANS activity. In these cases, it is noted how valence and arousal may affect the physiological variables related to the cardiovascular system in different ways.

It is pertinent to highlight that both valence and arousal were the most registered psychological variables in the selected studies. However, it is necessary to extend research focused on other aspects, such as anxiety and personality. Research with personality as an observed variable are probably less common, due to the complexity of its evaluation and conclusions over obtained results [32], [42]. Moreover, there is a lot of debate around this topic and it can add complexity to the studies that may arise. In this sense, anxiety could be also a useful element to consider in future research.

Scientific disciplines for documents sourced in this paper

In this review, studies from different scientific fields were included. The research chosen is associated with areas such as music therapy, work hygiene, music´s influence on the heart´s parameters and affective sounds. The scientific disciplines from which these studies are selected is shown in the Table 1. This paper has shown that the effects of sound on humans has been studied from diverse viewpoints, ranging from music therapy to work hygiene. However, the latter has been considered with more frequency. In the same way, Figure 9, summarizes how the effects of sound, noise and music on the human body may be studied from different aspects. These factors may impact both the mind and emotions as much as the body. This may be observed both psychologically and as a medical response. Hence, sound may be used to produce different outcomes in areas from music therapy and arts to work hygiene.

Table 1. Scientific disciplines for documents sourced in this paper

Scientific domain	Documents
Music therapy	9 10 33 46 47 48 50 51 52 60 63
Work hygiene	11 12 13 14 16 19 20 21 23 24 28 30 31 38 40 41 45 58 62 64
Music influence on heart parameters	5 15 17 18 22 27 29 37 53 54 56 65 68
Affective sounds	26 32 34 35 36 39 42 43 44 49 55 57 59 61 66 67 69 71

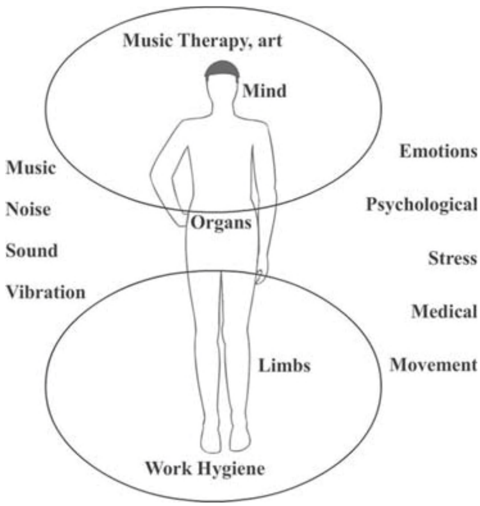

Figure 9. Influence of sound, noise and music on the human body

Limitations

One limitation in this review is related to the number of revisers. We think that in order to carry out the best review on this topic, it is necessary to have a multidisciplinary team with several researchers in each of the areas, such as, medicine, cardiology, psychology, music or music therapy, engineering, and statistics. Moreover, it is also considered that this may also introduce the possibility of bias in the selection of papers included in this review.

2.5. Conclusions

In this review, some relevant characteristics between selected studies were seen. Despite the differences between the outcomes of selected studies, some common elements were found among them. Thus, in noise studies where both BP and HR increased or tended to increase, it was noted HRV (HF and LF/HF) changes with both sound and noise stimuli, whereas GSR changes with sound and musical stimuli. Furthermore, LF also showed changes with exposure to noise. In many cases samples represented a limitation in experimental design, where in diverse studies there was a lack of a control group. Regarding stimuli, there was a great variability in the presented stimuli providing a wide overview of the effects they could produce on humans. In the listening sessions some elements which represent good practices in experimental designs were observed, such as the use of headphones, comfortable positions for study subjects, and control of environmental elements. Moreover, a minimum length of listening session of 20 minutes was found in most of research. However, this variable needs critical review and standardization for future research. The use of classic statistics had a dominant role in most studies. New data analysis tools should also be included. Besides ECG, in some studies, registers for other variables of the cardiovascular system were acquired which may support findings about the interest variables. It is important to mention that selected studies do not provide enough evidence about the influence of sound over ECG signal. In this sense, new research needs to be carried out which allow us to make conclusions about this topic. In this way, this review aims to provide elements which can contribute to improving quality in future research about sound and its effects over ECG signals.

An important point to consider, is the extensive variability in the research characteristics. Thus, there is little homogeneity among the elements, such as, stimulus, sample and experimental design in studies with sound, noise and music. The variations in these characteristics hinder the possibility to draw a complete conclusion with respect to the relationships between causes and effects. However, despite these variations, it was possible to observe some of the elements which were often present.

In sound and noise studies, it was noted that HF and HF/LF ratio HRV were elements with variations according to the provided stimuli. In the same way, GSR was an element which presented variations with sound stimulus and served as an element in classifying emotions in research with music.

This review shows that there is a genuine need to continue with research related to the influence of sound, noise and music on psychophysiological variables. It is known that noise can affect several aspects in humans, both psychological and physiological. However, studies of this review do not show a common trend. Therefore, it is important to consider future research to observe and understand the response to different types of noises, such as traffic noise.

In addition, it is important to highlight that future research needs to have a strict experimental design as well as to provide a complete report or publication about its outcomes. Thus, it is essential to bear in mind the suggestion to include stimuli with different characteristics in control groups. It is advisable to avoid control groups in silence or without some stimulus. In this way, it is necessary to understand the human response to stimulus with of a different nature, such as several types of sounds, noise and music [5].

To complement this review, we suggest reading the review "Music and the heart" by Stefan Koelsch and Lutz Jäncke [5]. The authors provide methodological recommendations for future research related to music (although many of them are suitable for research with sound and noise).

It is important to take into account the Consolidated Standards of Reporting Trials (CONSORT) [72] for randomized controlled trial designs, the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) [73] for non-randomized designs, Reporting Guidelines for Music-based Interventions [74] for music-based intervention studies and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [75] for reviews.

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Chapter III. Recognition of valence judgments in music perception using electrocardiographic signals and machine learning[2]

The medicine of the future will be
music and sound.

Edgar Cayce

[2] This section is a part of the published article by Ennio Idrobo-Ávila

Recognition of valence judgments in music perception using electrocardiographic signals and machine learning

3.1. Introduction

Stress may affect human beings in beneficial ways, preserving cell homeostasis [1] and enhancing the manner in which people learn and remember [2]. Chronic exposure to severe conditions of stress, however, can lead to a number of obstacles to human health. Stress disorders affect the central nervous system, immune system function, and the condition of the gastrointestinal, endocrine, and cardiovascular systems [1]. Stress can furthermore produce changes in heart-brain interaction [3]. Due to the role of stress in human health, physicians require a wide range of therapeutic tools for treatment. Pharmacological medication and nutraceuticals and non-pharmacological interventions are all relevant [1]. Non-pharmacological music interventions have shown a reduction in anxiety [4] and stress in psychophysiological variables [5] [6].

Research has examined how music may help with stress management. Music interacts with humans through their sentiments and emotions. The use of electrocardiographic signals (ECG) and heart rate variability (HRV) can help to assess states of stress [7–9] as well as emotions elicited by music [3] [10]. HRV revealed the varying music capacity for reducing stress [9] and how music could produce arousal responses and ease stress [11]. Pleasant and unpleasant music produced changes in periodic repolarization dynamics [12] [13]. ECG and galvanic skin response (GSR) were also considered in assessing the influence of sleep on emotional perception of music, revealing an association between emotion and sleep duration [14]. Another study showed that an increase in heart and respiratory rates occurred while subjects listened to happy music, whereas only heart rate increased with sad music; valence modified heart rate whereas arousal produced changes in respiratory rate [15].

Others used ECG and developed systems to classify different states or responses to music. Systems were developed for instance to recognize conditions before and after listening to music using: two musical genres [16]; responses to music with four different emotional characters [17]; and four emotional responses to music able to induce emotions related to four quadrants in the model of valence-arousal: joy, tension, sadness, and peacefulness [18]. Most research used classic statistical analysis tools [9,11–15], while others used machine learning tools such as k-means, naïve Bayes and artificial neural networks [16], probabilistic neural network [17], and least squares support vector machine [18].

The field of human-computer interaction (HCI) has not yet fully explored ECG as a measure for recognizing conditions of stress and emotions elicited by music. But examples in the literature include the following: A system for reducing human effort and improving the practicality of HCI was developed, comprising a music player that selects songs depending on the emotion of the user. The system recognized four emotions (happy, angry, sad and neutral) by means of facial expression, using convolutional neural networks [19]. Another system for playing notes on a musical score was developed, controlled by eye-tracker and head movements on fixing the gaze on a point on the score [20]. Elsewhere, a structure was created for multimodal control of musical performance and sonic interaction, through explicit interaction with tangible objects (pucks), and implicit interaction by measuring brain activity (electroencephalography-EEG) and ECG [21]. In other studies, physiological measurements were used to perform sound synthesis and control of tempo in a digital musical instrument, while a system was developed to detect emotion using EEG, pulse, and blood pressure, recommending color and music according to emotional states of users of a self-driving vehicle, classifying emotions by support vector machines [22].

However, since implicit interaction interfaces (e.g. that use physiological measurements) are still emerging, research is needed on such interfaces in HCI systems, to determine to what extent they might enhance human bandwidth in control or interaction [21]. The use of physiological signals to generate music automatically was thus proposed in the field of physiological computing [23]. Although physiological response elicited by music has been assessed using such signals as ECG and HRV [11] [16], most systems do not incorporate each subject's own perception. Most considered a two-dimensional emotion space [17]. Research carrying out the classification of emotions has generally used music previously categorized according to the emotion it is able to produce (emotional music). Emotions associated with sadness, peacefulness, and happiness have commonly been considered, together with emotions related to tension such as threat, scary, or fear [14,17,18,24]. There is room for improvement, as classification rates oscillate between 60 and 90% [18,22,25,26] in the best cases.

Our contribution

Given the above history, recognizing that ECG signals are seldom used for emotion recognition and that very little research has associated heart and emotions using machine learning [27], we have constructed a system to recognize or classify emotional responses to music and nature sounds, from ECG signals and using a single perception scale.

Our hypothesis is that emotional responses to such sounds, measured by a single scale, can be recognized using only ECG signals classified by machine learning techniques. For future applications to be able to take decisions aimed at reducing stress in subjects based on their emotional response, it is clearly important that machines can recognize states of stress. Further studies are also required regarding pleasant and unpleasant emotions elicited by music, an area of research “still in its infancy" [3] by which sounds and their influence could enhance the quality of human life. Similarly, physiology-based interfaces in HCI have also been suggested as a means of improving single- and multi-user experiences [21].

3.2. Methodology

3.2.1. Data acquisition and experimental procedure

Data acquisition required the participation of 23 healthy adult volunteers - 9 females and 14 males, with a mean age of 25.5 yrs (SD=6.8) - in an experimental auditive procedure. All gave informed consent. The ethical committee of the Universidad del Cauca approved the informed consent and the experimental procedures in their entirety. Subjects were assessed through an audiometry exam, and were fully instructed about the procedures of the experimental phase. For the presentation of auditive stimuli, subjects were in a supine position, equipped with noise-cancelling headphones (Figure 1) and instructed to keep their eyes closed. Their heart electrical activity was then recorded using an ECG acquisition system (OpenBCI - Cyton Biosensing Board (8-channels) [28]); the electrode position in the ECG corresponded to that of the lead II. ECG was recorded with a sample rate of 250 Hz. Each subject was tested individually.

Once the subjects were prepared, music and nature sounds were played randomly to them. The 11 music tracks comprised instrumental song sections; ten nature tracks made up the test. At the end of each track, the subjects opened their eyes and assessed their perception (by means of a graphical user interface projected on the ceiling above them) on a scale of 1 to 9, with low figures representing a negative response and higher figures reflecting a more positive reaction (these responses were then grouped in binary form – as “Positive” or “Negative” to carry out the subsequent classification). After subjects recorded their perception, a 15-second period of silence was incorporated before the next track. Volume was normalized across all tracks and each track comprised 12 seconds. Music included Colombian music from the Pacific coast, Latin Jazz, Merengue, Rock in Spanish, Classical, Bachata, Popular music, Vallenato, Reggaeton, and Ballads in Spanish. These genres were chosen given the experiment cultural context in Southwestern Colombia. The 21 tracks were played a single time, in a random manner, to each subject.

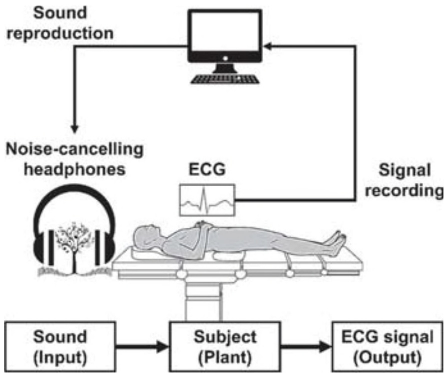

Figure 1. Diagram of experimental procedure

3.2.2. Signal processing

Captured signals (n=483) were conditioned by applying a third-order one-dimensional median filter and after that, filtered signals were subtracted from the original signals to perform baseline wander correction [29]. A data augmentation process was then carried out using wavelet-based shrinkage filtering [30]. Following the method implemented in [30], three mother wavelets were used to filter the signals - Daubechies 4 (db4), Daubechies 6 (db6), and Symlets 8 (sym8). The outcome of this process was 1932 signals. Signals were then segmented by means of a Hamming Window; each signal was divided into three segments of six seconds each, with 50% overlapping [31]. After that, feature extraction was conducted, where maximum, mean, variance, skewness, kurtosis, energy, entropy, and Katz and Higuchi (k=3) fractal dimensions of the signals were extracted; these features were computed directly from the signals. Feature extraction was carried out in Matlab software [32].

3.2.3. Classification

Having extracted the features, classification processes were implemented using six artificial intelligence algorithms: k-nearest neighbours (kNN), lightGBM, neural network, random forest, and XGBoost (Table 1). These were designed to discriminate between the binary perception responses: Positive and Negative.

Table 1. Configuration parameters of the implemented artificial intelligence algorithms

Classification algorithms	Configuration
k-nearest neighbours	Number of neighbours: 20, metric: Manhattan, weight: distance
LightGBM	Max bin=600, learning rate=0.001, number of leaves=12, boosting=gbdt, number of iterations=7000
Neural network	Multi-layer perceptron with backpropagation. Neurons in hidden layers: 90, activation: ReLu, regularization: alpha=0.05, solver: Adam
Random forest	Number of trees: 45
XGBoost	Learning rate=0.3, max depth=5, min child weight=1, gamma=0, alpha=0.1, subsample=1, colsample by tree=1, objective=multi:softprob

3.2.4. Data, training, test and evaluation of models

Regarding the dataset generated, the rate of positive and negative sentiments were 53% and 47% respectively for music, and 70% and 30% respectively for nature sounds. The ten folds cross-validation method was utilized for training the algorithms. Performance was evaluated using the area under the ROC curve (AUC), accuracy, precision, recall, and F1-score [33]. These metrics allow evaluation of classifier performance working on imbalanced datasets.

3.3. Results

After training the selected algorithms, performance was evaluated through the AUC, accuracy, precision, recall, and F1-score metrics. The classification evaluations are shown according to the type of stimuli considered - music (Figure 2) and nature sounds (Figure 3). The outcomes showed accuracy up to 0.86 and AUC 0.91 for music stimuli (Figure 2) and both accuracy and AUC up to 0.92 for nature sounds (Figure 3).

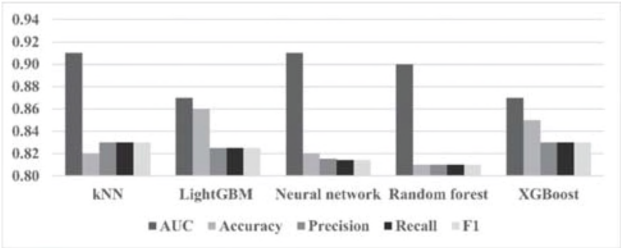

Figure 2. AUC, accuracy, precision, recall, and F1-score for music stimuli

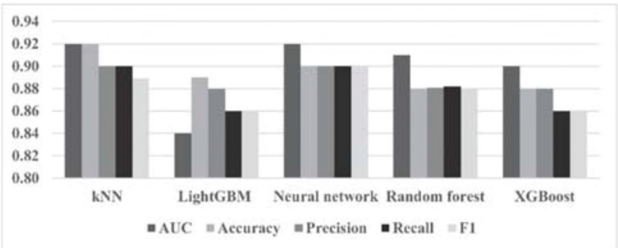

Figure 3. AUC, accuracy, precision, recall, and F1-score for nature sound stimuli

3.4. Discussion

From the outcomes it was observed that a single scale of emotion evaluation with a particular ECG signal lead allowed the selected machine learning algorithms to discriminate valence judgments elicited by music and nature sounds. With music stimuli, the best AUC performance was achieved with the kNN and neural network algorithms, both attaining 0.91, and accuracy was greatest using lightGBM, with an accuracy of 0.86. The best performance with nature sound stimuli was with kNN, with 0.92 AUC and accuracy, while neural network also achieved an AUC of 0.92. In general, classification of emotions elicited by nature sounds was better than with music (Figure 2 and 3), although this could be influenced by the unbalanced responses to nature sounds. All considered evaluation metrics confirm this higher performance, although AUC provides a more generalized view of the performance of the algorithms and the description of the studied phenomenon. This suggests that subjects responded more uniformly to nature sounds than to music. This behaviour may arise from the fact that people generally are exposed to the same common nature sounds, provoking more or less the same responses. People are exposed to music however in many different ways in their daily lives. Moreover, personal preferences and tastes have a great influence, producing more variability in the responses between subjects.

Discriminating between relaxed and excited states elicited by a multimedia exposure that incorporated relaxing and exciting music, 90% accuracy was achieved using GSR, ECG, electrooculogram, EEG, and photoplethysmography [25]. Another study, classifying three responses to Persian music - happy, peaceful, sad - attained an emotion classification accuracy of 90% [34]. While the above studies mainly classified responses to music associated with pre-anticipated emotions or emotions defined previously, in the present work, the emotional responses of subjects to a range of stimuli was considered, rendering remarkable the high performance in accuracy obtained. Even more remarkable given that the perception of each subject plays an important role in the classification.

Another study in the field of HCI classified four emotional states (stability, relaxation, tension, and excitement) from EEG data with a performance of 86% [22]. Similarly, other work classified music-evoked emotions from EEG data, in which 67% for valence was the best performance [26]. Meanwhile, in [18], for positive and negative valence, high and low arousal, and four types of emotion (joy, tension, sadness, and peacefulness) correct classification rates of 83, 73, and 62% were achieved, respectively. Our results correspond closely to the 83% valence classification. Differences were seen as subjects presented their perception report for each stimulus individually while in [18] subjects reported their perception after listening to longer sessions of several minutes in which several stimuli were presented. Additionally, our results suggest that with only 12 seconds it is possible to produce an emotional response in subjects. The comparative studies above considered EEG signals while in our experimentation, emotion recognition was performed using ECG signals.

New HCI proposals in physiological computing suggest the use of such physiological signals as EEG, ECG or electrodermal activity to automatically generate music using machine learning techniques. Our system represents an approximation to this aim [23]. Moreover, this type of system could be applied in the field of education where background music is expected to improve learning processes [10]. Applications in music therapy, stress management, the practice of yoga or mindfulness might also be implemented. New studies may even address the support of therapies to manage depression using implicit interaction (measuring ECG signals) in HCI systems based on music stimuli. A great advantage in systems that use ECG is its simplicity for measurements in comparison with physiological signals such as EEG. For very lite applications ECG could be measured using only two electrodes [35] [36].

3.5. Conclusions

A system based on machine learning techniques and ECG signals was designed, to recognize emotional responses to music and nature sounds, measured by a single scale of perception. Subjects were found to give more uniform responses to nature sounds than to music. The kNN algorithm gave the best mean performance. It was possible to recognize the distinctive perception of subjects using binary evaluation and ECG signals. These outcomes encourage new research and applications that take account of the individual perception of each subject in such a way that an HCI system based on music perception could operate in a more personalized way with more accuracy. This study showed that with a short period of exposure to a stimulus it is possible to elicit emotions in listeners. A recommendation for future work however concerns the exploration of longer stimuli; another recommendation involves the emotion evaluation scale, initially suggesting the inclusion of a neutral possibility in addition to negative and positive perception; finally, studies using more subjects are recommended, leading to more robust systems with a better performance.

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Chapter IV. Judgement of valence of musical sounds by hand and by heart, a machine learning paradigm for reading the heart

The human heart feels
things the eyes cannot see,
and knows what the mind
cannot understand

Robert Valett

... and listens to sounds
the ear cannot hear.

Judgement of valence of musical sounds by hand and by heart, a machine learning paradigm for reading the heart

4.1. Introduction

The electrocardiogram is a record over time of the heart electrical activity; this activity is registered as an analogue signal known as the electrocardiographic signal (ECG) [1]. Because of its ambulatory character and simplicity in comparison with other medical procedures, ECG is the most common heart medical exam [2]. It is often used as an indicator of the physiological condition and as a diagnostic tool of the cardiovascular system, in particular of the heart health [3]. Among other models of ECG analysis, heart rate variability (HRV), derived from the R-R interval peaks of ECG, emerges to reveal relationships between autonomous neuron system and physiological, physical or psychological variables [4]. HRV exposes the interplay between the sympathetic and parasympathetic nervous system [5]. HRV has been applied to study cardiovascular diseases such as acute ischemic stroke [6], cardiac autonomic dysfunction [7], cardiopulmonary dysfunction [8], myocardial infarction [9], and cardiac death [10]. HRV has been considered to assess panic disorder [11], mental health resilience [12], and depressive disorder [13]. The effects of electronic cigarette [14], exercise [15] [16], and alcohol use [17] have been also evaluated using HRV.

In the same way, HRV has also been employed to assess the effects of sound and music on the heart [18], where research on this topic has gained importance in the recent time since it makes it possible to understand and take advantage of the music benefits [19] [20], as the decreasing in the heart rate and in the systolic and diastolic blood pressure [21]. Thus, music has been studied from several perspectives. For instance, in the direction of multimodal music information, several tasks have been developed, among them it is possible to find music segmentation, emotion or mood recognition, synchronization of different representations, and classification of music [22]. In like manner, some researchers have developed systems based on deep learning to create music [23]. In addition to fields as Computational Musicology [24] and Interactive music [25], the use of music in health sciences has also been examined to manage several diseases or conditions such as autism [26], depression [27], cancer [28], and cardiovascular diseases [20].

Besides a lot of applications of the ECG and HRV in the clinical domain and research, they have been used to analyse how music with different emotional character affects the heart [29] [30] [31], and some of these studies have been carried out with both musicians [32] as non-musicians [29]. Although the effects of music on heart behaviour have been studied, research has not established the best way of audio stimulation [18] and because until now it is still unclear which musical element is related to the observed changes, it is required to develop systematic high-quality research on the effects of music on the heart [33]. In this aspect, most of the previous research has focused on the effects produced by the tempo of music [34 35 36]. Literature reports a great variation of the effects of music on HRV, avoiding the possibility to draw substantial conclusions [18]. Previous research has classified the HRV response to old generation romantic music with a performance of 80% of accuracy, using artificial neural network [37]. Another research classified the response of the Autonomic Nervous System with the HRV to Odia and Tamil music [38]. The classification used the Regression Tree, Boosted Tree and Random Forest algorithms and a performance of 85% was achieved. From previous studies, it is observed that is required to develop classification systems of HRV responses to sound stimuli to improve the performance of previous studies.

Consequently, this study assesses in more detail the effects of harmonic intervals on the heart response. Additionally, it evaluates the heart reaction to noise stimuli. To achieve this goal, some machine learning techniques were considered to make associations between stimuli and heart responses and compared with the judgements of the subjects on the valence of the sounds. These techniques were selected considering recent experimentations that have done the data analysis throughout artificial intelligence tools [19 37 39 40]. This study hypothesizes that the selected sound stimuli can produce different responses in the heart. It is hypothesized that heart responses can be classified according to the sound stimuli using algorithms of machine learning.

The remainder of this document is organized as follows: Section 2 presents a description of the methods where the experimental procedure and data processing are shown; Section 3 reports the results, where the most salient outcomes can be observed; Section 4 covers discussion of the results; and finally, Section 5 shows the conclusions of this study.

4.2. Methods

4.2.1. Experimental procedure

Participants

Participants were voluntarily enlisted in the experiment, 26 healthy subjects without vocational music training, 17 males and 9 females, with an average age of 25.3 years old (SD=7.1), ranged from 18 to 37 years. The participants underwent audiometry exam to ensure they could hear well. They were asked to sleep well, not to consume either caffeine or alcohol, not to practice sports or to consume stimulant substances 24 hours before sample collection. All procedures were carried out considering the Declaration of Helsinki to keep the safety and confidentiality of subjects. All procedures, including experimentation on human subjects, were approved by The Internal Ethical Committee of Universidad del Cauca, and the research was done according to the approved protocol.

Sounds

In this experiment, 30 different stimulus conditions of two different types were used: noise, and harmonic music intervals (HMI). The noise and HMI signals were synthesized in order to have as much control as possible in the stimulus presentation. The noise stimuli taken into account were: blue, brown, grey, pink, purple and white noise. The HMI type consisted of the all possible harmonic intervals in one octave, including two different octaves: a lower since A2 to A3 and a higher between A4 and A5. Each musical note was composed of more than one partial frequency, i.e. complex tones; as partial frequencies increased, their power decreased. The power spectrum and timbre of the harmonic sounds synthesized were similar to the flute. All these intervals had the A2 and A4 as the low notes, while the higher ones were changed. Thus, stimuli had the intervals in two octaves, octave 2 and 4: minor second (2m), major second (2M), minor third (3m), major third (3M), perfect fourth (4), augmented fourth (4aug), perfect fifth (5), minor sixth (6m), major sixth (6M), minor seventh (7m), major seventh (7M), octave (8). To avoid the influence of changes in the volume and the intensity sound, the perceived loudness was normalized in all sounds by applying ReplayGain [41]. The responses to the used stimuli were analysed from the following aspects as type (noise and HMI), frequency (high and low), consonance and dissonance (HMI), and as independent stimuli (**Table 1**).

Table 1. Description of the employed stimuli

* 1-12: lower octave; 13-24: higher octave

Type	Index*	Description	Frequency Class	Consonance Class	Instances
Harmonic intervals (HMI)	1 - 13	Minor second (2m)	Low: Octave 2 High: Octave 4	Dissonant	5616 (234 per each stimulus)
	2 - 14	Major second (2M)		Dissonant	
	3 - 15	Minor third (3m)		Consonant	
	4 - 16	Major third (3M)		Consonant	
	5 - 17	Perfect fourth (4)		Consonant	
	6 - 18	Augmented fourth (4aug)		Dissonant	
	7 - 19	Perfect fifth (5)		Consonant	
	8 - 20	Minor sixth (6m)		Consonant	
	9 - 21	Major sixth (6M)		Consonant	
	10 - 22	Minor seventh (7m)		Dissonant	
	11 - 23	Major seventh (7M)		Dissonant	
	12 - 24	Octave (8)		Consonant	
Noise	25	Grey	Low and High	---	1404 (234 per each stimulus)
	26	White	Low and High		
	27	Brown	Low		
	28	Pink	Low		
	29	Blue	High		
	30	Violet	High		
Total					7020

In addition to consonant and dissonant analysis, the sounds were studied in three and nine classes according to the perception scores of subjects. In three classes, a negative class was defined with scores between one and three, while the positive class took scores between seven and nine; in addition, a neutral class was defined with scores between four and six. Finally, in nine classes each set of scores was considered as an independent class, i.e. one class per score, from one to nine.

Data collection

The procedure was made in an isolated room from external stimuli, with an average temperature of 23°C, sound pressure level of 40 dB, and illumination of 100 Lux. Before the procedure, once the research and its purposes were explained, the participants signed the consent form. The experiment was conducted with one subject at a time, who reminded isolated, and in a comfortable stretcher. The subjects were in a rest supine position for 15 minutes and after this period they were equipped with Bose Noise Cancelling Headphone 700 and they were also asked to close their eyes to avoid the influence of any visual stimuli. At once, a baseline was measured for two minutes. Following this time, 30 sounds were played in random order; 24 sounds with harmonic intervals in the octaves 2 and 4, and six different noise sounds. These sounds were played during ten seconds each and were separated by a silence section of 15 seconds. The subjects were instructed to score their perception about the listened sound immediately each sound had finished; then they should have opened their eyes, score their perception on a screen projection in front of them, and closed their eyes again. The procedures were designed to avoid the effort of subjects, reducing the need to speak and move. Subjects registered their perception by using a Bluetooth mouse in a user interface, on a scale between 1 and 9, where 1 represented the worse (Negative) reaction or perception related to the stimuli and 9 was the best one (Positive). They were instructed to follow the instruction: "Please, rate your experience after each sound on a scale from 1 to 9; negative experiences will be rate with low numbers and the positives will be with higher values". During the complete procedure, it was measured the lead II of the ECG signal by using the Cyton OpenBCI board [42]. All tests were made between 15.00 and 18.00 hours in order to reduce the influence of the circadian cycle in the heart function.

4.2.2. Data processing

The complete procedure to collect data had four different stages: pre-processing, dataset augmentation, feature extraction, and classification; in addition, a feature ranking stage was made. As a first step, the ECG captured signals were pre-processed; in this procedure, the baseline was removed by applying a third-order one-dimensional median filter and after that it was subtracted from the original signal. Pre-processing of ECG signals is carried out to get a clean ECG signal, by reducing the effects of adverse factors such as Gaussian noise, muscle artifacts, power-line interference, and baseline wander, where baseline wander is a noise source with frequency content less than 1.5 Hz [43]. R-peaks were segmented by using the Pan-Tompkins algorithm [44]; undetected peaks were marked manually. This segmentation is carried out to extract the HRV signal [45] through the time difference between R-peaks, by measuring R-distances in milliseconds [46]. Data augmentation was implemented by applying circular shift and hyperspectral data augmentation; these procedures were applied with the methodology described in [47] and [48] [49], respectively. As results of these processes, the order of the RR intervals is changed, and noise is introduced in the principal components of the data. The dataset original had 780 instances and after the data augmentation process was incremented to 7020. Data augmentation is a very useful technique to generate more samples from which algorithms can learn improving their accuracy, as well as overfitting can be reduced and generalization increased [50] [51].

Feature extraction and reduction of dimensionality

After the pre-processing and data augmentation stages, a feature extraction process was realized from each signal segment. In the feature extraction process, temporal, frequential and non-linear domain features were considered from the HRV. The extracted features represent in a compressed form the HRV data, depicting behaviours or patterns from different domains such as time and frequency (**Table 2**). Details about HRV features could be found in this reference [52]. In the analysis, independently of their physiological interpretation, selected features are considered as descriptors of ECG signals. After the feature extraction, in order to reduce dimensionality in the extracted features, it was done a ranking of the best features with the scoring method Information Gain Ratio [53]; from the ranking process, the 11 best-ranked features were chosen to apply the classification process. The number 11 was selected with respect to a classification analysis with the best features (See below: Section 3.2.2. Harmonic intervals - Classification with the best-ranked features: HMI classes, 24 harmonic intervals). Reduction of dimensionality is carried out to suppress redundant or irrelevant variables; this helps to improve prediction accuracy and reduce the computational cost in training processes, as well as allows a better understanding of data [54].

Table 2. Complete set of HRV features

HRV features
Higuchi fractal dimension (k=2)
Higuchi fractal dimension (k=3)
Higuchi fractal dimension (k=4)
Hurst exponent
Katz fractal dimension
HRV detrended fluctuation analysis alpha 1
HRV detrended fluctuation analysis alpha 2
mean of the heart rate
mean R-R interval
performing triangular interpolation
triangular index from the interval histogram
root mean square of the successive differences
minor semi-axes of the ellipse fitted in the Poincaré plot (SD1)
major semi-axes of the ellipse fitted in the Poincaré plot (SD2)
ratio between the axis of the ellipse fitted in the Poincaré plot (SD1/SD2)
correlation dimension
approximate entropy
low-frequency components
power of low-frequency components
power of high-frequency components
ratio of low and high-frequency components
high-frequency components
very low-frequency components
total power
probability of intervals greater 50ms
interquartile range of Euclidean distance
median of Euclidean distance

Classification and evaluation

This research considered four machine learning algorithms to carry out the classification tasks: AdaBoost, k-nearest neighbours, Neural network, and Random forest (**Table 3**). The configuration parameters were chosen by experimentation.

Table 3. Configuration parameters of the classification algorithms

Classification algorithms	Configuration
AdaBoost	Base estimator: Tree, Number of estimators: 50, Learning rate: 1, Classification algorithm: SAMME.R
k-nearest neighbours	Number of neighbours: 20, metric: Manhattan, weight: distance
Neural network	Multi-layer perceptron with backpropagation. Neurons in hidden layers: 90, activation: ReLu, regularization: alpha=0.05, solver: Adam
Random forest	Number of trees: 45

The training and evaluation process of the model was done through the cross-validation, by considering ten folds. Cross-validation was applied based on the subjects; this procedure was applied five times and the mean of these outcomes was reported. This method reduces the randomness from splitting the data only once, reduces the overfitting, and increases the replicability of the outcomes [55]. Additionally, the Matthews Correlation Coefficient (MCC), sensitivity, specificity, accuracy, and – AUC – area under the ROC curve (receiver operating characteristics) were taken as assessing metrics. The MCC is a metric to assess the performance of predictors or classifiers and it is very useful since it could be used even with imbalanced data; a value of 1 means an ideal prediction, -1 represents a total inverse prediction, and 0 is related to random processes [56]. In this research, the link between HRV and the administered stimuli was done throughout the classification of several features extracted from HRV signals. In this case, considering the experimental design, a good classifier performance, represented by high scores in the assessing metrics, can be associated with a relation cause-effect between the stimuli and heart response, measured by HRV signals; in this case, the MCC metric is presented as one of the most favourable to describe the studied phenomenon.

4.3. Results

This section presents the results of two ways of analysis. The first one studies the response of the heart to two different stimuli, i.e., noise and harmonic intervals; the second analysis shows a deeper view by considering the different types of noises and harmonic intervals separately.

4.3.1. Noise and harmonic music intervals

As a first analysis, it was performed a classification of the stimulus types, i.e. noise, and harmonic intervals from sets of features of the HRV signal and using four different classifiers (**Figure 1**). From the outcomes is possible to see that in general, the classification algorithms are able to differentiate between the classes of noise and HMI. Except for AdaBoost classifier, the performance in this classification was equal to or higher than 0.84 in all metrics considered. MCC and AUC are very important in this classification since this is carried out on an imbalanced dataset.

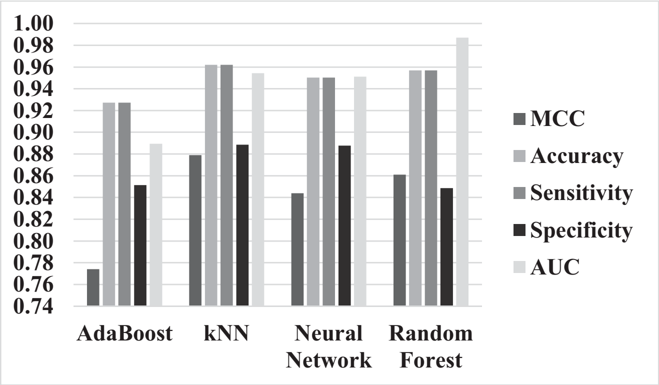

Figure 1. Classification performance of the type of classes (stimuli): noise and harmonic intervals (**Table 1**)

4.3.2. Noises and Harmonic intervals as independent classes

Once the study with two classes ended, to take a closer observation into the stimuli of noise and harmonic intervals, it was done an analysis with one type of class at once, i.e. noise and harmonic intervals separately.

4.3.2.1. Noise

The first analysis with one type of sound was done with the noise class. It was realized with the Frequency Class of Table 1 (**Figure 2**) and by classifying the six different types of noise used in this research (**Figure 3**). Except for AdaBoost classifier, the performance in classification tasks with noise was equal to or higher than 0.85 in all metrics considered. In these classifications is observed that specificity is higher than sensitivity which suggests that the algorithms have more probability to detect true negatives than true positives (**Figure 2** and **3**).

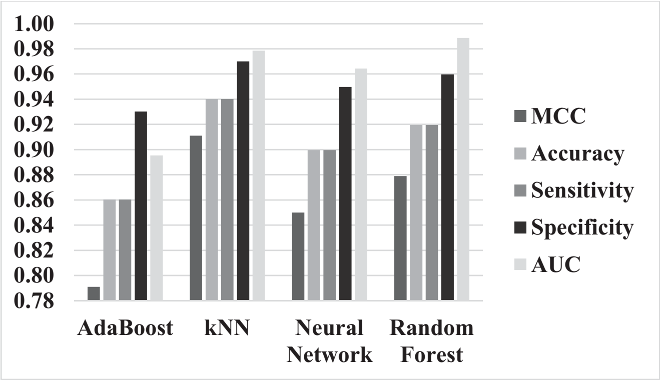

Figure 2. Classification performance of the noise classes: low, high, and low-high band frequencies (**Table 1**)

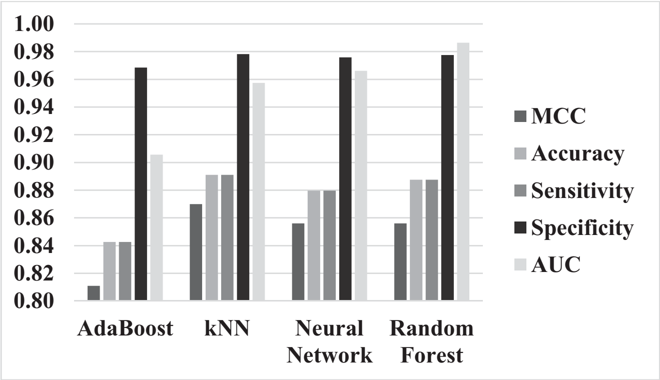

Figure 3. Classification performance of the noise classes: Blue, Brown, Grey, Pink, Purple and White noise (**Table 1**)

4.3.2.2. Harmonic intervals

After the analysis of noise, the harmonic intervals in three different aspects were studied (**Table 1**): low and high frequency (**Figure 4**), i.e. octaves 2 and 4 respectively, consonant and dissonant (**Figure 5**), and each interval separately (24 classes, **Figure 6 and 7**). Except for AdaBoost classifier, the performance in classification tasks with harmonic intervals was equal to or higher than 0.80 in all metrics considered. Unlike previous results - Figure 2 and 3 - the outcomes in Figure 4 and 5 show similar levels in sensitivity and specificity, i.e. the similar probability to detect true negatives than true positives. Contrary to this, the results in Figure 6 are similar to Figure 2 and 3, where detection of true negatives has more probability than true positives.

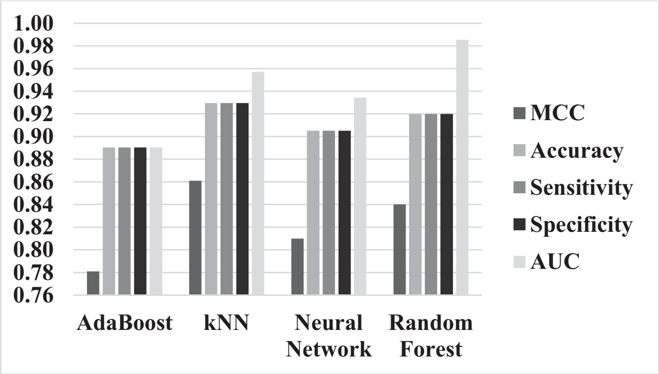

Figure 4. Classification performance of the HMI classes, octaves 2 and 4 with harmonic intervals (**Table 1**)

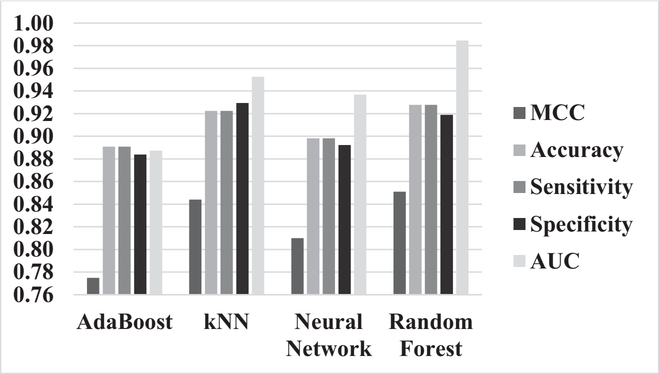

Figure 5. Classification performance of the HMI classes, consonance and dissonance (**Table 1**)

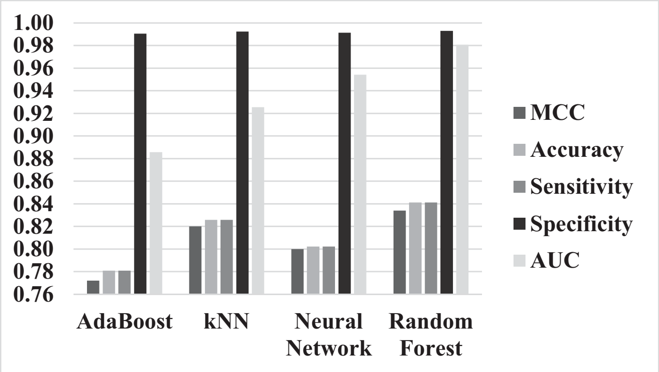

Figure 6. Classification performance of the HMI classes, 24 harmonic intervals (**Table 1**)

Classification with the best-ranked features: HMI classes, 24 harmonic intervals

Within the analysis of each interval separately, classification performance according to the number of the best-ranked features is presented (**Figure 7** and **Table 4**); this analysis was carried out by considering the Random forest classifier since this was the algorithm with the best general performance in the whole study, and the metrics accuracy and MCC. This analysis was carried out to observe the impact of using different numbers of features in the classification performance and, to show what features might be more affected by the stimuli; HMI in this case.

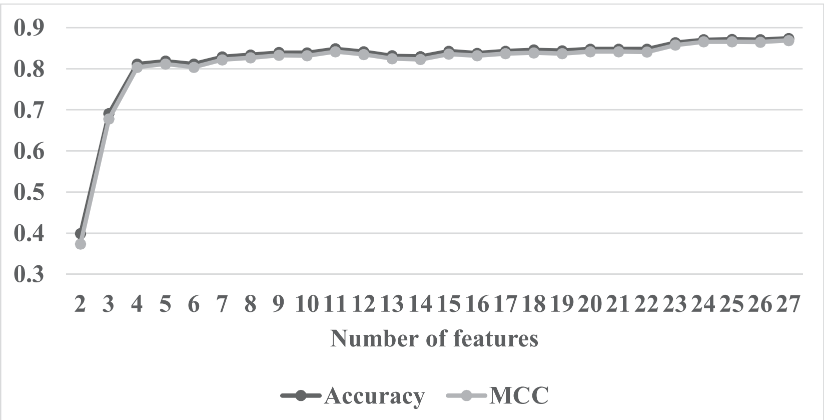

Figure 7. Random forest classification with ranked features: HMI classes, 24 harmonic intervals (Table 1)

Table 4. Ranking of HRV features using information gain ratio (IGR)

Ranking	HRV feature	IGR	Ranking	HRV feature	IGR
1	Higuchi fractal dimension (k=4)	0.0340	14	ratio of low and high-frequency components	0.0214
2	performing triangular interpolation	0.0315	15	root mean square of the successive differences	0.0210
3	high-frequency components	0.0312	16	Katz fractal dimension	0.0209
4	major semi-axes of the ellipse fitted in the Poincaré plot (SD2)	0.0270	17	triangular index from the interval histogram	0.0207
5	total power	0.0269	18	interquartile range of Euclidean distance	0.0204
6	low-frequency components	0.0262	19	Higuchi fractal dimension (k=3)	0.0194
7	probability of intervals greater 50ms	0.0256	20	correlation dimension	0.0192
8	median of Euclidean distance	0.0248	21	Hurst exponent	0.0184
9	ratio between the axis of the ellipse fitted in the Poincaré plot (SD1/SD2)	0.0241	22	approximate entropy	0.0171
10	Higuchi fractal dimension (k=2)	0.0238	23	mean of the heart rate	0.0135
11	minor semi-axes of the ellipse fitted in the Poincaré plot (SD1)	0.0222	24	mean R-R interval	0.0133
12	power of low-frequency components	0.0214	25	HRV detrended fluctuation analysis alpha 1	0.0094
13	power of high-frequency components	0.0214	26	very low-frequency components	0.0059
			27	HRV detrended fluctuation analysis alpha 2	0.0045

4.3.3. Perception analysis

In addition to the discrimination between the different types of sounds, the capacity to separate the sound according to the perception of subjects was also studied. Both ignoring the class of sound when considering the sound type (noise and HMI, **Figure 8**). This analysis considered the classes listed in the section 2.1. Experimental procedure - Sounds. Since these classification tasks were carried out on unbalanced datasets, the performance evaluation is presented based on the Matthews correlation coefficient (MCC) for all of the classifiers. These classifications were accomplished with 3 and 9 classes of perception, on the different considered stimuli - Noise and HMI, Noise, and HMI independently. The MCC for classification performance was equal to or higher than 0.80. The best performance was achieved by the Random forest classifier, where the highest MCC value – 0.94 - was achieved with noise stimuli and the scale with 9 values for perception.

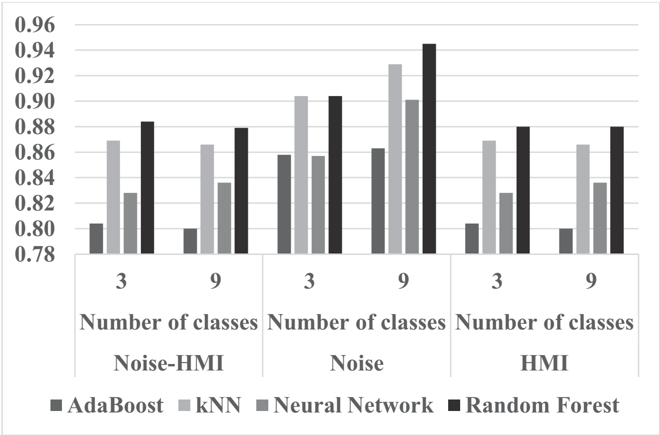

Figure 8. Matthews correlation coefficient of the sound perception classification with three and nine in relation to all stimuli (noise and HMI), noise, and HMI (**Table 1**)

4.3.4. Descriptive statistics of the HRV features

After the classification analysis, descriptive statistics of the HRV features were implemented in order to make observable the changes of the HRV features according to the presented stimuli (**Table 1**). The Kruskal-Wallis statistic-test was used to determine if there were significant differences between the features [57]; a p-value less or equal to 0.05 was considered to be statistically significant (**Table 5**).

Table 5. Descriptive statistics of the HRV features according to the presented stimulus

Feature		Class		p-value
		Noise	Harmonic intervals	
Higuchi fractal dimension (k=2)	Mean±SD	1.72±0.40	1.64±0.39	0.001
	Median	1.68	1.61	
probability of intervals greater 50ms	Mean±SD	0.38±0.15	0.35±0.14	0.004
	Median	0.38	0.36	
ratio between the axis of the ellipse fitted in the Poincaré plot	Mean±SD	0.97±0.31	0.92±0.32	0.001
	Median	0.92	0.83	
		Harmonic intervals		
		Consonant	**Dissonant**	
Higuchi fractal dimension (k=3)	Mean±SD	1.91±0.37	1.86±0.33	0.001
	Median	1.87	1.76	
ratio between the axis of the ellipse fitted in the Poincaré plot	Mean±SD	0.94±0.32	0.90±0.30	0.001
	Median	0.85	0.78	
ratio of low and high-frequency components	Mean±SD	0.59±0.29	0.62±0.32	0.022
	Median	0.47	0.55	
		Valence		
		Negative	**Positive**	
Higuchi fractal dimension (k=2)	Mean±SD	1.60±0.36	1.74±0.43	0.001
	Median	1.57	1.68	
Higuchi fractal dimension (k=3)	Mean±SD	1.84±0.36	1.98±0.43	0.001
	Median	1.79	1.92	
mean of the heart rate	Mean±SD	0.93±0.14	0.97±0.11	0.001
	Median	0.96	0.95	

4.3.5. Results of the subjective valence judgements of the musical sounds

In parallel the subject judged the degree they felt the presented sound was more positive or more negative (i.e. in valence). They were asked to express this on a scale of 1 (negative) to 9 (positive).

In order to present sounds that would differ in valence we have constructed harmonic musical intervals different in pitch distance. These intervals have in the musical practice different degrees in consonance or dissonance, which in theory would differ in valence. The intervals were presented in two spectral positions: one low in the range of the male voice and one two octaves higher. Furthermore, some noise bands that differ in the point of gravity of their spectrum were added. The valence of all these stimuli can be compared with the spectrum of the familiar sounds in human speech [58].

As the subjects did not all use the same part of the response scale their values were normalized by subtracting the mean and dividing them by the standard deviation of their judgements. This way we became a judgment matrix of the sounds versus the subjects.

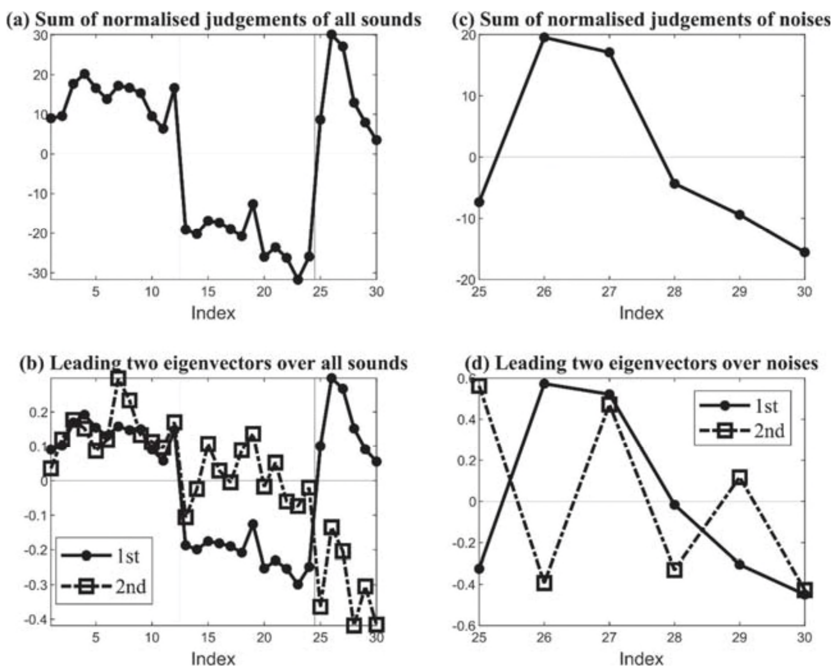

Figure 9. Valence judgements of stimuli

In Figure 9 and 10 the valence judgements are given as summed over all the subjects after normalisation. In Figure 9, the top left subplot (a) presents the ratings over all sounds in three sections, intervals in low octave (index 1 to 12), intervals in high octave (index 13 to 24), and noises (index 25 to 30); the sounds are presented in the same order of that of Table 1. It is very clear that the intervals in the lower octave (index 1 to 12) and the noises (index 25 to 30) are rated positive, and the intervals in the higher octave (index 13 to 24) are rated negative. The first two right singular vectors presented in the bottom left subplot (b) of the SVD of the judgement matrix indicate two different processes: 1. the difference in spectral position of the harmonic intervals, and 2. the dependence on the precise interval. In subplot of the top right (c), it is possible to see that also in the judgements of the valence of the noise bands have a maximum in position 26 and 27 and taper off towards low and high frequency bands. From the first two right singular vectors (bottom right, d), which is nearly the same as the overall judgement it is clear that there is only one process is happening: the spectral position.

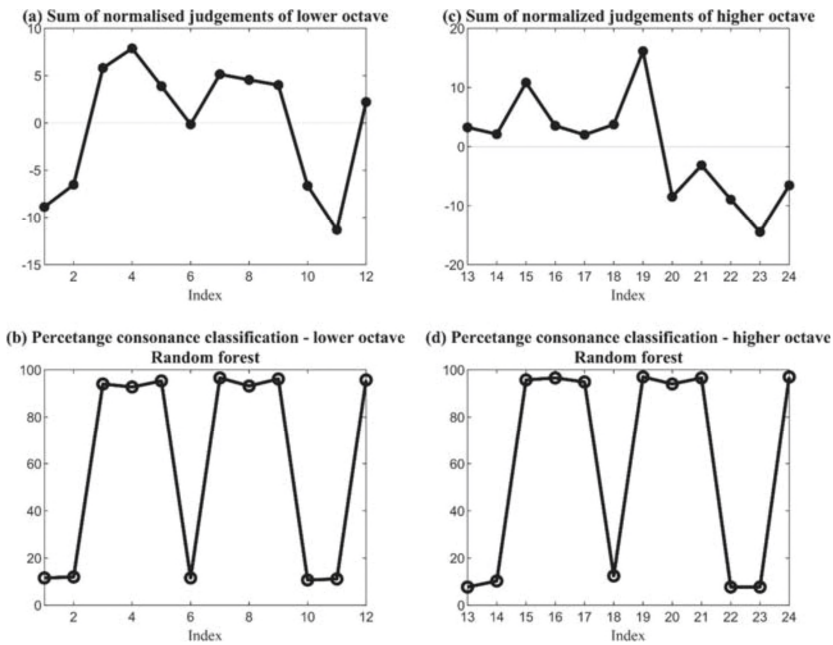

Figure 10. Valence judgements of HMIs

In Figure 10, the top left subplot (a) shows the judgments of the HMI in the low octave. The indexes also represent the distance in semitones between the two tones of the harmonic intervals. The intervals with 3, 4, 5, 7, 8, and 9 semitones are rated positive, the interval 1, 2, 10, and 11 as negative. The tritone of 6 semitones is rated as 0. This corresponds quite well with the theory on consonance. The machine learning classification (random forest) of heart response to consonance and dissonance intervals in the low octave agreed very well with subject perception (bottom left, b). The top right subplot (c) reveals that the higher valence goes with lower recognition of the consonance intervals. Only the minor third and the fifth jump out. In the high octave, while subject perception was not closer to the consonance theory as in the low octave, the machine learning classification (random forest) of heart response was as similar as the observed in the low octave, following completely this theory (bottom left, d).

4.4. Discussion

This research studied the effects of the harmonic intervals in two separate octaves and in addition to some types of noise on the activity of the heart, HRV features. In this case, it was searched a heart response related to specific elements of music; harmonic intervals and, noise sounds were included as a variation in the stimuli. The outcomes showed the heart response after ten seconds of exposition to the stimuli; this duration of stimulus exposition was similar to the reported in the IADS-2 database [59].

In fact, there is an influence of the selected stimuli over the heart behaviour, specifically in some features of the HRV. At this point, it is important to mention that despite most of the HRV analyses have been done in the long-term, some of these features in short-term recordings [60] have also been carried out. In this study, HRV measures were extracted from ECG signals along ten seconds duration with a main purpose to describe the signals in question. In this case, this short-term response in HRV was related to the interpretation in the long-term; however, it is important to clarify that it is required the validation of this association and to study which ultra-short HRV features can be considered as good descriptors [61]. This is an exploratory study to determine if there is a heart response - HRV - to harmonic musical intervals and coloured noise

The results also showed that it is possible to discriminate with high accuracy the heart response to two different types of stimuli: noise and harmonic intervals. It is also possible to infer that the heart behaviour connected to these stimuli has a complex nature, so it is necessary to take several features in order to classify the response with MCC higher than 0.84 (except for the AdaBoost classifier, **Figure 1**). As a consequence, this is a multidimensional task. The results suggested the heart behaviour of the subjects was influenced in a different way by the different types of sounds used in the experiment. With a descriptive statistical analysis, it was possible to observe that Higuchi fractal dimension (k=2), probability of intervals greater 50ms, and ratio of standard deviation 1 and standard deviation 2 of the Poincaré plot had higher values in the condition of noise than in the condition of HMI ($p < 0.005$). It is observed that unordered sounds (noise) produced different responses in comparison with ordered sounds (HMI); noise incremented the fractality respect to

HMI. It would be interesting to determine in future research if this behaviour is reproducible with other types of ordered and unordered sounds.

After the analysis of two classes, a deeper examination was performed with one class of sound, i.e. the noises and the harmonic intervals were studied individually. First, in the noise class, it was discriminated the response to the sound in relation to its frequency content (**Table 2**), namely low, high, and low-high bands (all frequency bands) and regarding the noise types. In both cases, it was reached an MCC higher than 0.85 (except for the AdaBoost classifier, **Figure 2** and **3**). These results meant the heart behaviour changed with each noise of diverse frequential content or type; i.e. different types of noise, according to their frequency bands, produced distinct effects on the heart.

As a second part of the examination, with one class of sound, the Harmonic music intervals (HMI) were analysed; heart responses were classified regarding stimulus characteristics such as frequency content – low and high octave -, consonance – consonance and dissonance -, and as individual sounds – 24 HMI - (**Figures 4, 5,** and **6**). In all cases, it was reached an MCC superior to 0.80, except for the AdaBoost classifier. The success of these classification processes suggests the heart response was affected in a different way by the octave of the sounds (high or low frequency), their consonant or dissonant nature, and by each harmonic interval sound independently.

The feature ranking in the process of classification of each interval separately revealed the extent of the contribution to this task of each feature in turn (**Table 4**). As might be expected, the very low-frequency components made no contribution because of the duration of the HRV record/analysis (10 seconds); additionally, it is important to note how the mean of the heart rate and the mean R-R interval also each contributed little to this classification. Bearing this in mind, it would be possible then to say that the HMI stimuli did not produce changes in the heart rate and the mean R-R interval. The first four or five features meanwhile made the biggest contribution to the classification process, since with these it was possible to achieve metrics of accuracy and MCC higher than 0.8. In this light, features such as Higuchi fractal dimension (k=4), high-frequency components, and total power made a substantial contribution to this discrimination task; it would thus be fair to state that the HMI stimuli produced bigger changes in these features.

The analysis with descriptive statistics (**Table 5**) showed in this case that Higuchi fractal dimension (k=3) changed from 1.86 for dissonant to 1.91 for consonant intervals ($p = 0.001$). Unlike than noise stimuli, ordered sounds – consonant - incremented the fractality respect to less ordered sounds - dissonant. The ratio between the axis of the ellipse fitted in the Poincaré plot varied from 0.90 for dissonant to 0.94 for consonant intervals ($p = 0.001$). The ratio of low and high-frequency components decreased its values from 0.62 to 0.59 for dissonant and consonant intervals ($p=0.022$), increasing the parasympathetic dominance [45] (assuming the validity of this ratio for short-term HRV). Finally, regarding of heart response to valence perception, the Higuchi fractal dimension ($k=2$) and mean of the heart rate increased from 1.60 to 1.74, and 0.93 to 0.97, respectively. These results might be a possible inspiration for future research in such a way specific sounds such as harmonic music intervals can be used to produced controlled changes on HRV and heart response.

Regarding sensitivity and specificity, in the case of different types of classes/stimuli, or unbalanced datasets, sensitivity was greater than specificity (**Figure 1** and **5**). In the case of discrimination of classes belonging to the same type, sensitivity was equal to or less than specificity (**Figure 2, 3, 4,** and **6**). In the classification of 24 harmonic intervals (**Figure 6**), due to the number of classes in this task, specificity tends to take greater values than in problems with few classes; in this case, due to the fact that the algorithms are dealing with a balanced dataset, accuracy provides a better metric of performance.

The heart response was also analysed (**Figure 8**) to the sounds regarding the perception of subjects; this procedure was done by including all the types of sounds, i.e. noise and HMI. In this procedure, the positive, negative, and neutral perception distributed in 3 and 9 classes were considered. In this last case, it was observed that the perception has considerable relevance in the heart response since MCC>=0.8 was achieved in all classifications considering or not the type of the stimuli. Thus, it could be possible to infer that the perception of sound has also an important influence on the effect of the sound in the heart behaviour, and, until a certain point, it could be independent of the type of noise or harmonic intervals.

In respect of the experimental design, the HMI stimuli had the same lower tones, 110 and 440 Hz, both in the lower and in the higher octaves. This fact introduced those notes as a reference for the ear; where a modal or even tonal perception could be introduced in the listeners. I.e. a tonality around the root A - A2 and A4 - could be perceived by the subjects. This general condition could have introduced a bias in the outcomes into the heart response to these HMI. For this reason, it is important to include HMI with different lower notes in future studies. It would be also interesting to determine if the observed heart responses are also observed in HMI stimuli in different octaves than those included in our experimental design, i.e. lower and higher than 2 and 4.

The judgements of the subjects confirmed the relation between valence and consonance (**Figure 10**). The intervals in the higher octave were judged as less positive indicating the relation with the range of the human voice. The analysis of the heart signals revealed that aspects such as type of sound, frequency content, consonance condition (for HMI), and subjective perception had influence in the heart response to the sound stimuli. Each type of noise and harmonic interval itself originated a distinguishable reaction in the heart. It was possible to recognise the valence judgements by the heart response. While the classification of consonant/dissonant HMI matched with subject judgments, consonant related to positive and dissonant associated with negative.

The subjective perception of subjects agreed closely with the "actual" consonance/dissonance quality of the HMI stimuli in the lower and higher octaves (**Figure 10**), i.e. subjective perception did indeed have an influence on heart activity. However, it is important to remark that heart activity (HRV/ANS) was also affected not by subjective perception but by physical features of sound, specifically consonance and dissonance characteristics. In this case, there was no direct interaction between physical features of sound and the subjective perception of sound, in other words the heart reacted to consonant sounds similarly to the way in which it might react to other consonant sounds, independent of whether these were subjectively perceived as positive or pleasant. Despite the fact that these findings remain to be confirmed and expanded in future research, they anticipate a promissory tool with which to influence heart activity objectively, so that on determined occasions the subjective perception of listeners might well be discounted in order to standardize procedures or protocols concerned with affecting the heart with sound.

With this research was learned that considered sound had an influence on heart behaviour. Heart responses agreed with the subject judgements; this was very observable in the low octave of HMI sounds. Positive judgments were associated with heart response to consonant sounds and negative judgments to dissonant. An association of heart response with the frequency content of stimuli was observed. In addition to the better agreement between subject judgments and consonance/dissonance quality in the lower octave, algorithms found distinguishable heart responses between low and high HMI. Heart responses were also distinguishable by the algorithms between low, high, and low-high band frequencies of the noise stimuli. Since the heart might be influence by the consonant quality of HMI, and this response agrees with subject perception (valence), this research supports the theory related to the biological influence in the perception of HMI as consonant or dissonant [58]. It is important to note the fact that the noise stimuli were judged in the same range as the stimuli in the low octave. This represents a strong argument for the biological basis of valence.

From the outcomes, it is possible to observe that heart response to sound stimuli was affected by several elements implied. First, the type or nature of the sound produced different responses in the heart (**Figure 1**). Second, the frequency content of the sounds generated distinct heart reactions (**Figure 2** and **4**). Here there is an interesting element to study in future works, where it is important to determine if the heart response to frequency content depends or not of the sound type. Third, each sound in itself was able to produce particular reactions on the heart (**Figure 3** and **6**), where a better distinction in such reactions was noted with the noise sounds (**Figure 3**). Fourth, in the particular case of harmonic music intervals, their grade of consonance/dissonance contributed to the changes in the heart (**Figure 5**). Sixth, the experimented perception of subjects also contributed to heart reactions (**Figure 8**). Thus, heart response to sound stimuli was influenced by these six factors; a great capability of affectation and sensibility of heart to stimulus characteristics and perception of subjects was observed. Bearing this outcome in mind, in future research it is interesting to discover new factors that might influence the heart reaction to sound stimuli.

4.5. Conclusions

In this research, it was possible to establish differences between the heart response to sound noises and harmonic intervals by using tools of machine learning. With these tools was possible to determine that HRV features had the ability to represent the heart response to the selected stimuli. Aspects such as type of sound, frequency content, consonance condition (for HMI), and subjective perception had influence in the heart response to the sound stimuli. Thus, each type of noise and harmonic interval itself originated a distinguishable reaction in the heart. In the particular case of the harmonic intervals, it is interesting to note how the effect of consonance quality could be also found in the heart response. This study found support for a heart response to harmonic music intervals and coloured noise beyond the conscious processing of the subject. This fact involves a biological basis of valence and the perception of HMI as consonant or dissonant.

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Chapter V - Conclusions - a synthesis

Music can change the world

Ludwig van Beethoven

Conclusions

A methodology based on digital signal processing and artificial intelligence was designed to assess the effects of musical structures on electrocardiographic signals. First, a literature review was carried out to determine the characteristics of demographic samples, listening sessions, commonly encountered sounds, and analysis tools employed in earlier research related to musical structures and their influence on ECG signals. This review provided the foundations for the experimental design implemented during all stages of this study. Having completed the literature review, a methodology was developed for reproducing audio stimuli, capturing signals and analysing ECG signals in the domains of time and frequency by using digital signal processing and AI techniques. During this stage, an experimental protocol to assess the effects of musical structures on ECG signals was proposed. Finally, the methodology was evaluated once more with a new analysis to recognise valence judgments in music perception using ECG signals and machine learning techniques. It is worth noting that direct comparison with other studies was not possible here, as no databases were found in the literature related to heart responses to coloured noise or harmonic music intervals in two different octaves.

This research provided quantitative evidence that the considered sounds produced responses in the electrical activity of the heart. Techniques of digital signal processing and artificial intelligence such as machine and deep learning were able to prove that the heart reacted in a different way to different stimuli. It was observed in particular that different types of noise, harmonic music intervals, and instrumental sections of music generated different patterns in the captured ECG signals recognized by the techniques used in the analysis processes. These outcomes represent a valuable contribution to the fields of health and perception.

The reaction of the heart to the different types of noise reveals the influence of the frequency content of the stimuli. This fact was also observed with the recognizable response to the harmonic music intervals (HMI) in two different octaves - low and high. In addition to heart responses to each HMI, the consonance quality of the selected HMI stimuli was differentiable. This outcome was matched with the valence perception of the subjects, thereby presenting new support for the biological theory related to the appreciation of consonant and dissonant intervals. The instrumental sections of music showed particular reactions in the hearts of the listeners. This fact and the responses to HMI stimuli represent an important element that ought to encourage new approaches in the future of music therapy.

For future, continuing with this research is recommended, to place this knowledge within real contexts. With the implementation of applications in real environments, it is possible to take advantage of the multiple benefits that sound and music stimuli might produce on the health of people. From the engineering viewpoint, it is important to continue with this type of research in which the support to multiple disciplines such as perception, medicine, psychology, and arts might produce promissory outcomes.

Chapter VI – Annexes

Listen to your heart.
It knows everything.

Paulo Coelho

VI.a. Overview of the music theory related to this research

6.a.1. Harmonic series [1]

Every tone, with the exception of a pure sine wave, is made up of a composite of tones. These tones are called overtones, partials, or harmonics and constitute a series called the "harmonic series". The harmonic series is the set of partials that vibrate simultaneously when a natural tone is played. The strength or amplitude of a partial is usually determined by its placement within the series; the closer to the fundamental, the stronger the partial. The frequency ratios of the just intonation system (where the correct size of all the intervals of the scale is calculated by different additions and subtractions of pure natural thirds and fifths) occur naturally within the harmonic series. The following series of pitches will result from the partial vibrations of a C note, in which the pitches are shown as an approximation in the occidental tempered scale (Figure 1):

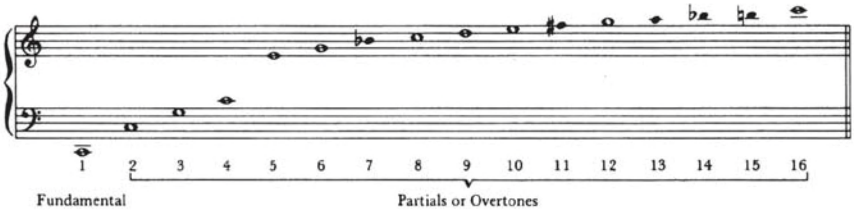


Figure 1. Series of pitches resulting from the partial vibrations of a C note

6.a.2. Overview of the music theory of harmonic music intervals [2]

An interval is the distance between two musical notes. There are two types of intervals: melodic and harmonic (Figure 2). A melodic interval refers to two notes that are played one following another, while the harmonic interval is related to two notes played at the same time.

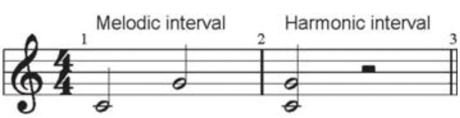


Figure 2. Melodic and harmonic intervals

Since the chromatic scale in western music has 12 different notes per octave (Figure 3) [3], it is possible to produce 12 different harmonic intervals in each (Figures 4). An octave is the distance between two notes where the fundamental frequency of the higher note is exactly twice of the lower [3].

Figure 3. The 12 notes in Western music

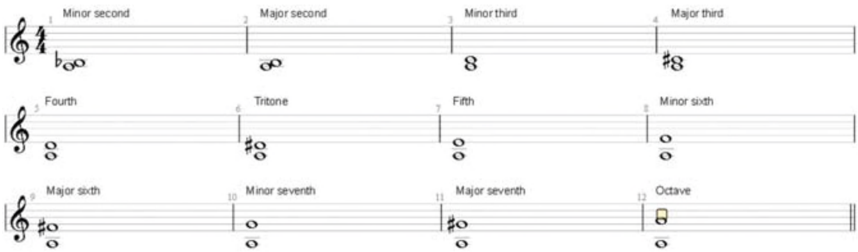


Figure 4. Chromatic intervals in one octave

An interval is perceived as more or less pleasant (in musical terms, consonant or dissonant) depending on its nature [4]. One of the most well-known theories put forward to explain the reason for consonance/dissonance perception is the ratio between fundamental frequencies of the notes which constitute the intervals. Thus, the simplicity of the frequency ratios determines the consonance quality; the simpler the ratio between two notes, the more consonant the sound (Table 1) [4].

Table 1. Consonance ordering of tone combinations

Interval evaluation	Interval name	Short name	Interval ratio
Absolute consonances	Unison	P1	1:1
	Octave	P8	1:2
Perfect consonances	Fifth	P5	2:3
	Fourth	P4	3:4
Medial consonances	Major sixth	M6	3:5
	Major third	M3	4:5
Imperfect consonances	Minor third	M3	5:6
	Minor sixth	M6	5:8
Dissonances	Major second	M2	8:9
	Major seventh	M7	8:15
	Minor seventh	M7	9:16
	Minor second	M2	15:16
	Tritone	TT	32:45

It is important to note that the theory presented emerges from within the context of the occidental culture, and this might change significantly with respect to the diverse oriental music. Likewise, this research is framed in an occidental context, both regarding the harmonic music intervals and the music used as stimuli. Thus, the obtained results cannot be completely generalized to the different cultures in the world.

VI.b. Musical Instrument Digital Interface (MIDI) [5]

MIDI is a protocol of communication that allows interaction between different compatible devices - commonly keyboards and computers. MIDI was developed by musical instrument manufacturers, among them Yamaha, Roland, and Korg) in 1983.

MIDI is not only a tool that has been used in the music industry but has also been implemented in medical areas [6]. Bearing in mind its great capacity of interaction and standardization, MIDI was used in the present research as a piano roll representation. In addition, the proposed biofeedback system is proposed with a strong base in the use of MIDI sounds. In this way, it is possible to generate a better interaction between the feedback system and the generation of audio.

VI.c. The process of perception of sound and music

The cochlea (Figure 5) is a spiral chamber of bone in the inner ear that converts or transduces the acoustic vibrations in the air to electrical signals [7]. The cochlea is home of the basilar membrane, a sheet covered with sound-sensitive 'hair cells'. When these cells are stimulated by acoustic vibrations, pores in the cell walls are opened. These pores allow the flow of charged metal atoms into the surrounding fluid, changing the electrical state of the cell. This procedure generates electrical signals that are transported by a nerve to the brain, where they are processed.

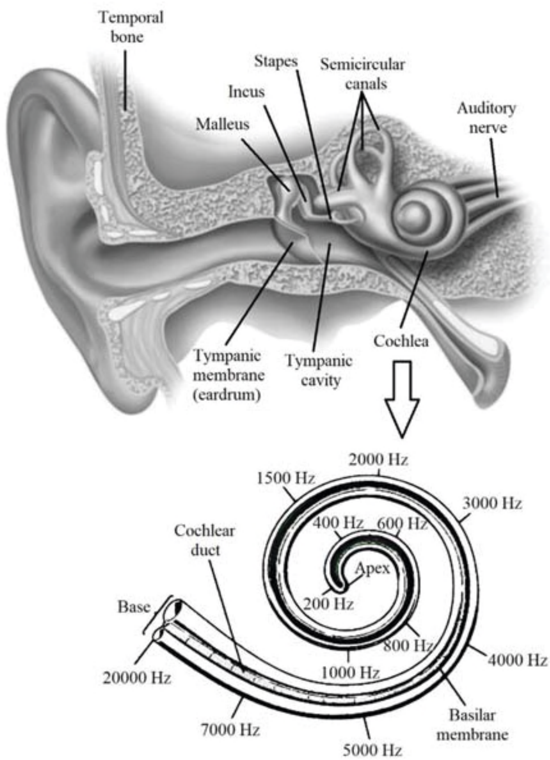


Figure 5. Anatomy of the ear (Image modified from [7])

Each of the hair cells responds to sounds with a specific frequency [7]. Those cells are in a basilar membrane arranged progressively, similarly to piano strings; cells that resonate with low-frequency sounds are at one extreme and those that resonate with high-frequencies are at the other end.

The description presented is related to the anatomy of the ear and represents the basis of auditory cognition, a process in which the sound is transformed into electrical signals. The sound perception is fully related to how those signals are processed. An initial process is linked with pitch. It appears that the basilar membrane has a set of neurons in the brain dedicated to decoding the membrane activity. The neurons that process pitch are in the primary auditory cortex and represent a special case, since there is a one-to-one mapping in the brain; there are no similar neurons that react to specific stimuli such as tastes, smells or colours [7].

In general, it is possible to say that music perception functions in three phases [8]: an elementary structural analysis (pitch, intensity, rhythm, duration, timbre), advanced levels (phrasing, timing, themes) and identification of music. Different brain regions are involved in each of these phases of perception [8]. In general, timbre and melody are processed in the right hemisphere, while rhythm and pitch are analysed in the left, generating interaction with the language areas [9]. It has been also observed that the perception of music produces activity in different cerebral regions depending on the musical education of the listeners; while in inexpert listeners, music activates the right hemisphere, in musicians it is activated in the left hemisphere [9].

Musical activity - listening, performing, and composing - has the capability to produce responses in several brain regions (Figure 6) [10]. The encoding of pitch height is performed in the primary auditory cortex, pitch height is processed in the posterior regions of the secondary auditory cortex and pitch chroma is processed in the anterior regions. Musical intervals have produced responses in the right temporal region, left dorsolateral prefrontal and right inferior frontal cortex; the superior temporal gyrus and planum polare are activated by intervals, contour, and melody. Rhythm perception and production involve regions in the cerebellum, basal ganglia, premotor cortex and supplemental motor area.

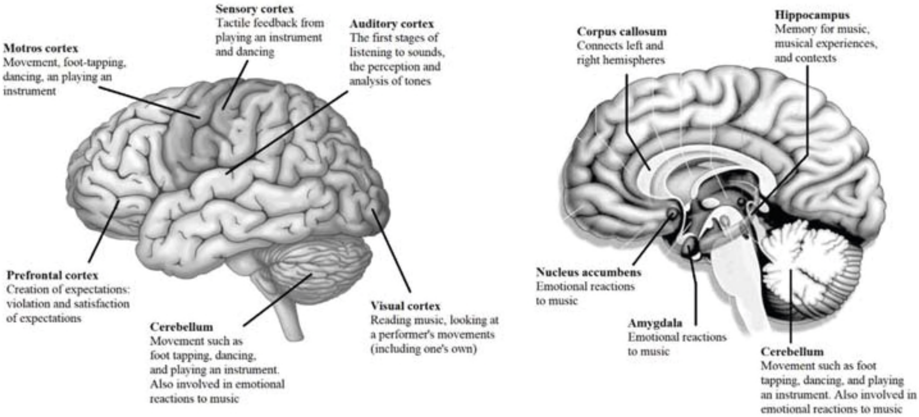


Figure 6. Brain regions associated with musical activity (Image modified from [10])

VI.d. Scientific manuscripts related to this book

VI.d.1. Journal Publications

1. *Idrobo-Ávila E. H., H. Loaiza-Correa, L. van Noorden, F. G. Muñoz-Bolaños, and R. Vargas-Cañas. "A proposal for a data-driven approach to the influence of music on heart dynamics", Frontiers in Cardiovascular Medicine, 2021.* *https://www.frontiersin.org/articles/10.3389/fcvm.2021.699145/full*

2. *Idrobo-Ávila Ennio, Humberto Loaiza-Correa, Flavio Muñoz-Bolaños, Leon van Noorden, and Rubiel Vargas-Cañas. "Judgement of valence of musical sounds by hand and by heart, a machine learning paradigm for reading the heart", Heliyon, 2021.* *https://www.sciencedirect.com/science/article/pii/S2405844021016686*

3. *Idrobo-Ávila E. H., H. Loaiza-Correa, L. van Noorden, F. G. Muñoz-Bolaños, and R. Vargas-Cañas. "Development of a biofeedback system using harmonic musical intervals to control heart rate variability with a generative adversarial network". Biomedical Signal Processing and Control, 2021.* *https://www.sciencedirect.com/science/article/pii/S1746809421006923?dgcid=author*

4. *Idrobo-Ávila Ennio, Humberto Loaiza-Correa, Flavio Muñoz-Bolaños, Leon van Noorden, and Rubiel Vargas-Cañas. "Can the application of certain music information retrieval methods contribute to the machine learning classification of electrocardiographic signals?", Heliyon, 2021.* *https://www.sciencedirect.com/science/article/pii/S2405844021003625#*

5. *Idrobo-Ávila E. H., H. Loaiza-Correa, L. van Noorden, F. G. Muñoz-Bolaños, and R. Vargas-Cañas. "Different types of sounds and their relationship with electrocardiographic signals and the cardiovascular system: A review." Frontiers in Physiology, 2018.* *https://www.frontiersin.org/articles/10.3389/fphys.2018.00525/full*

Accepted Journal Papers

6. *Idrobo-Ávila E. H., H. Loaiza-Correa, L. van Noorden, F. G. Muñoz-Bolaños, and R. Vargas-Cañas. "Heart response to harmonic music interval stimuli via deep learning", IJASEIT - International Journal on Advanced Science, Engineering and Information Technology, 2021.*

VI.d.2. Science communication: Presentations

7. *Idrobo-Ávila E. H., H. Loaiza-Correa, L. van Noorden, F. G. Muñoz-Bolaños, and R. Vargas-Cañas. "Heart response to harmonic music interval stimuli via deep learning", Ibero-American Conference on Software Engineering and Knowledge Engineering, Santiago, Chile, September 2021.*

8. *Idrobo-Ávila, Ennio, Humberto Loaiza-Correa, Rubiel Vargas-Cañas, Flavio Muñoz-Bolaños, and Leon van Noorden. "Recognition of valence judgments in music perception using electrocardiographic signals and machine learning". VI Ibero-American Conference on Human-Computer Interaction, Arequipa, Peru, September 16 - 18, 2020. CEUR Workshop Proceedings.*
   http://ceur-ws.org/Vol-2747/
   http://ceur-ws.org/Vol-2747/paper6.pdf

VI.e. Authors' biographies

Humberto Loaiza

Humberto Loaiza received the electrical engineering and automatic M.Sc. degrees from Universidad del Valle, Colombia, in 1990 and 1995. He received the PhD degree in robotic and computer vision from Université d'Évry, Francia, in 1999. He is currently a full professor of the School of Electrical and Electronic of the Universidad del Valle. From 2000, he is co-director of the Percepción y Sistemas Inteligentes (PSI) Research Group. His research interests include computer vision, digital signal processing, pattern recognition and mobile robotic.

Leon van Noorden

Leon van Noorden, 1945, Maastricht, NL. 1970, Technical Physics, and 1975, PhD on temporal coherence in auditory perception, Eindhoven TU. Worked for the Blind and the Post and Telecoms in the Netherlands and 20 years for the European Commission in Brussels in usability engineering and multi-media in broadband communications and as sector head in the funding and coordination of research and development of Digital Television. Joined in 2005 IPEM, University of Ghent, Belgium, as visiting professor to study synchronization of music and movement. Cooperates with Universidad del Cauca. He is also musician.

Flavio Muñoz Bolaños

Flavio Muñoz Bolaños received the Bs. in Biology and Chemistry in 1988 at Universidad Pedagógica y Tecnológica, Tunja, Colombia. Then, in 1996 a M.Sc. in Physiology, at Universidad del Valle, Colombia. Followed by a Postgraduate Diploma in Physical Therapy Activity, in 2011 at Institución Universitaria Escuela Nacional del Deporte, Colombia. Currently, he is a professor in General Physiology and Systems in Health Faculty at Universidad del Cauca, Colombia. His research interests include cardiovascular physiology, physiology of exercise, respiratory physiology, music and arterial pressure.

Rubiel Vargas Cañas

Rubiel Vargas Cañas received the Bs. Eng in Computer Sciences in 2000 at Universidad Industrial de Santander, Colombia. Followed by a M.Sc. in Engineering. Majoring in Electronic Engineering, in 2010 at Universidad del Valle, Colombia. Lastly, he received his Ph.D. degree in Biomedical Engineering in 2012 at City University, United Kingdom. Currently, he is a professor in computer sciences at Universidad del Cauca, Colombia. His research interests include digital signal and image processing, pattern recognition, machine learning, bioengineering, electronics, acoustics, music, and physics.

VI.f. A musical gift for science and music lovers: Al-Qamar (The Moon)

Music by Ennio Idrobo-Ávila. A musical piece inspired by the Andalusian and Arabian cultures, adopting the solemn style of Soleá and mixing modern and traditional elements of flamenco and Arabic music. The piece evokes the mystery behind moonlit nights, in which the dark blue sky enchants the imagination of people who surrender to limitations of the senses and attempt to escape by means of the illusion of a dream.

Image designed by

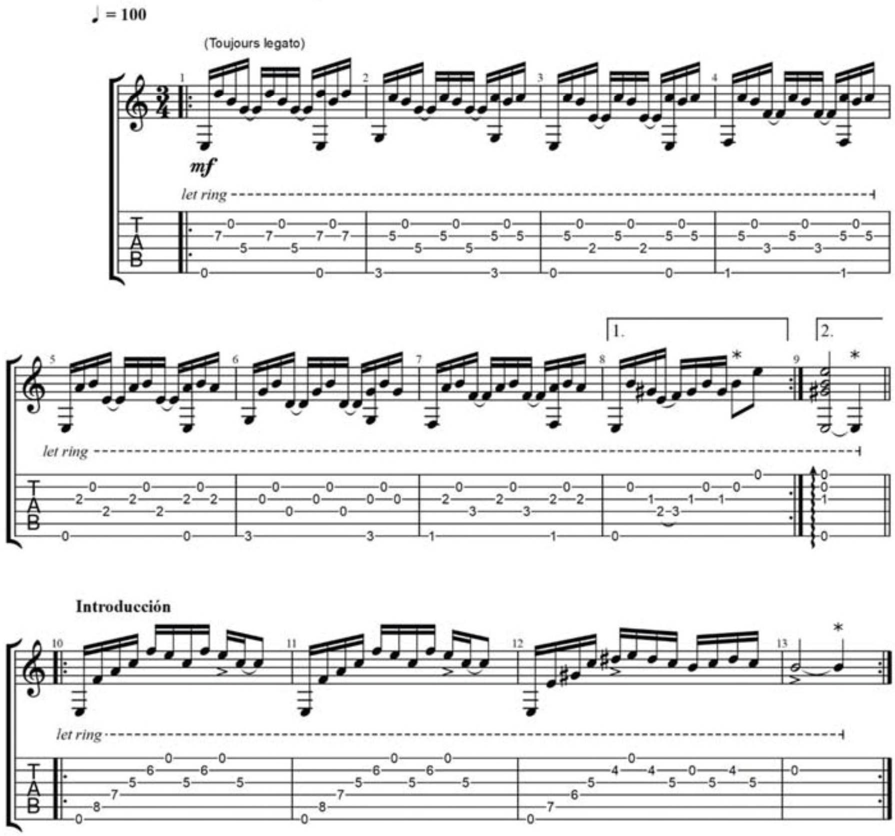
Fanny Rodriguez-Lozano,
Melany Moloney-Rodriguez,
Colin McLachlan, and
Ennio Idrobo-Ávila

Al-Qamar

de la Sonatine pour Marie: Soleá 2019:2021

Ennio Idrobo-Ávila

pour Liza María-Candamil



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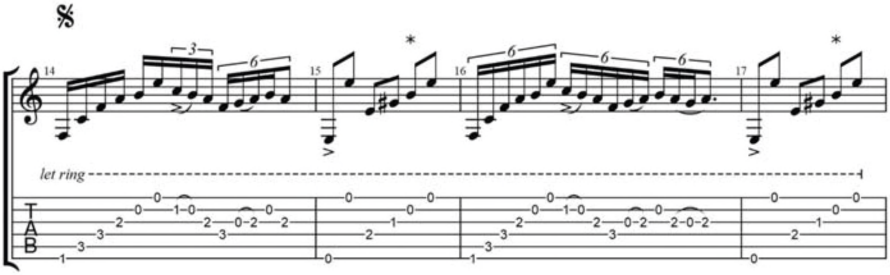

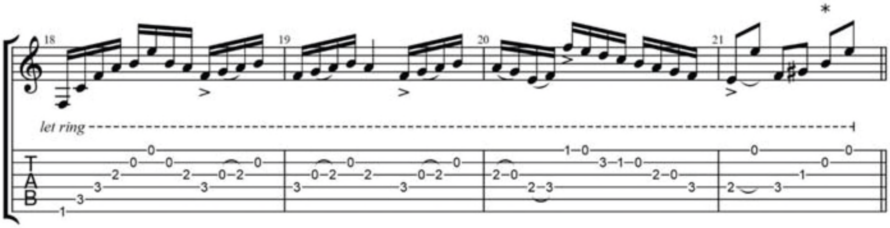

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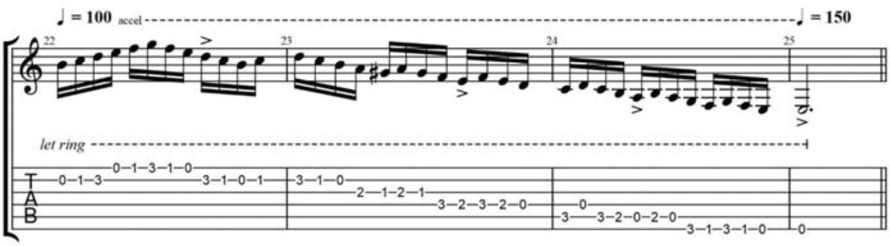

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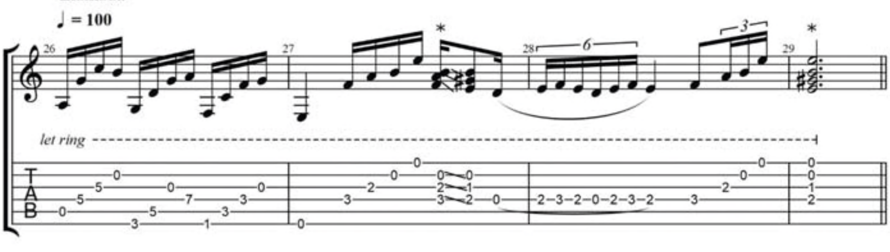

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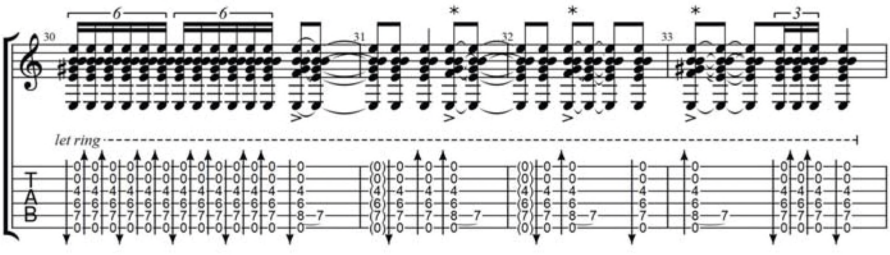

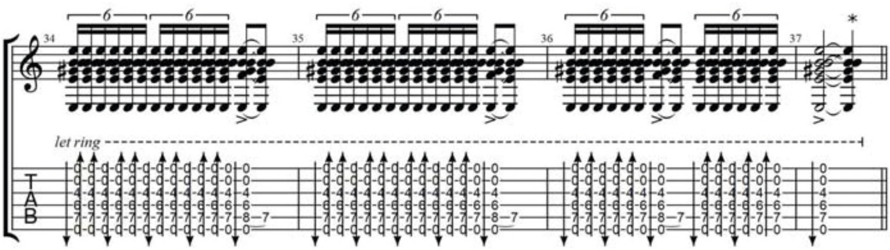

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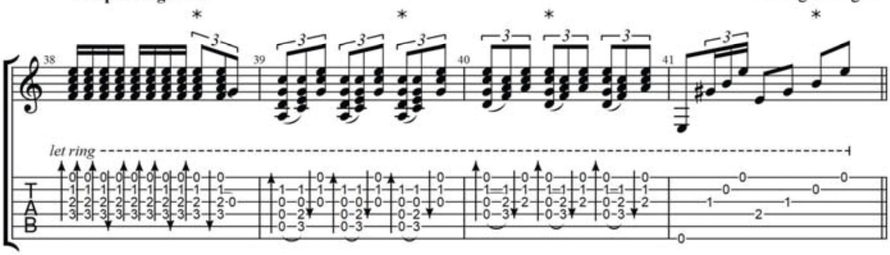

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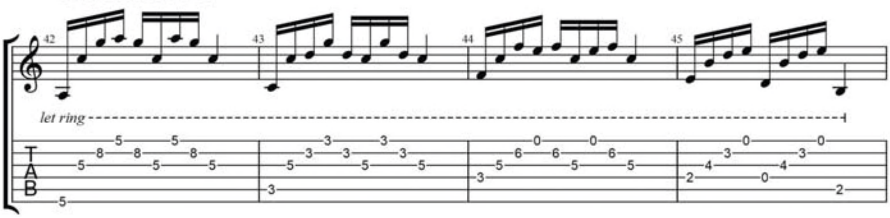

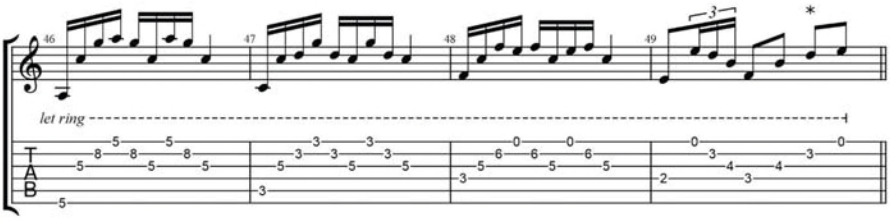

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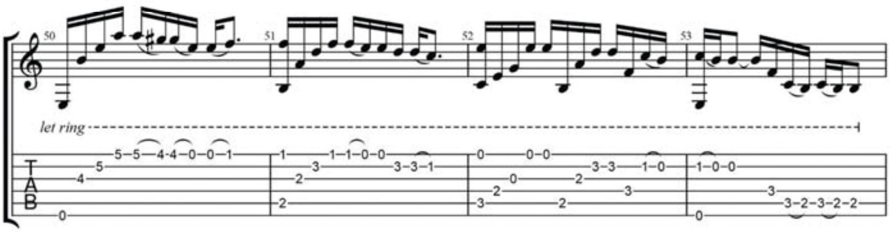

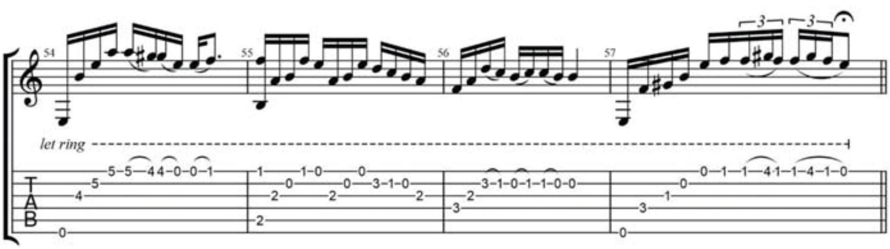

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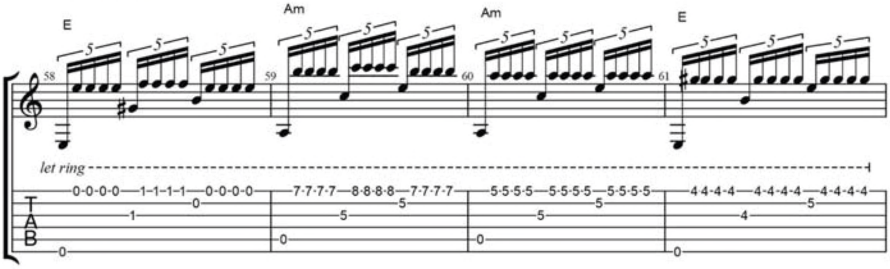

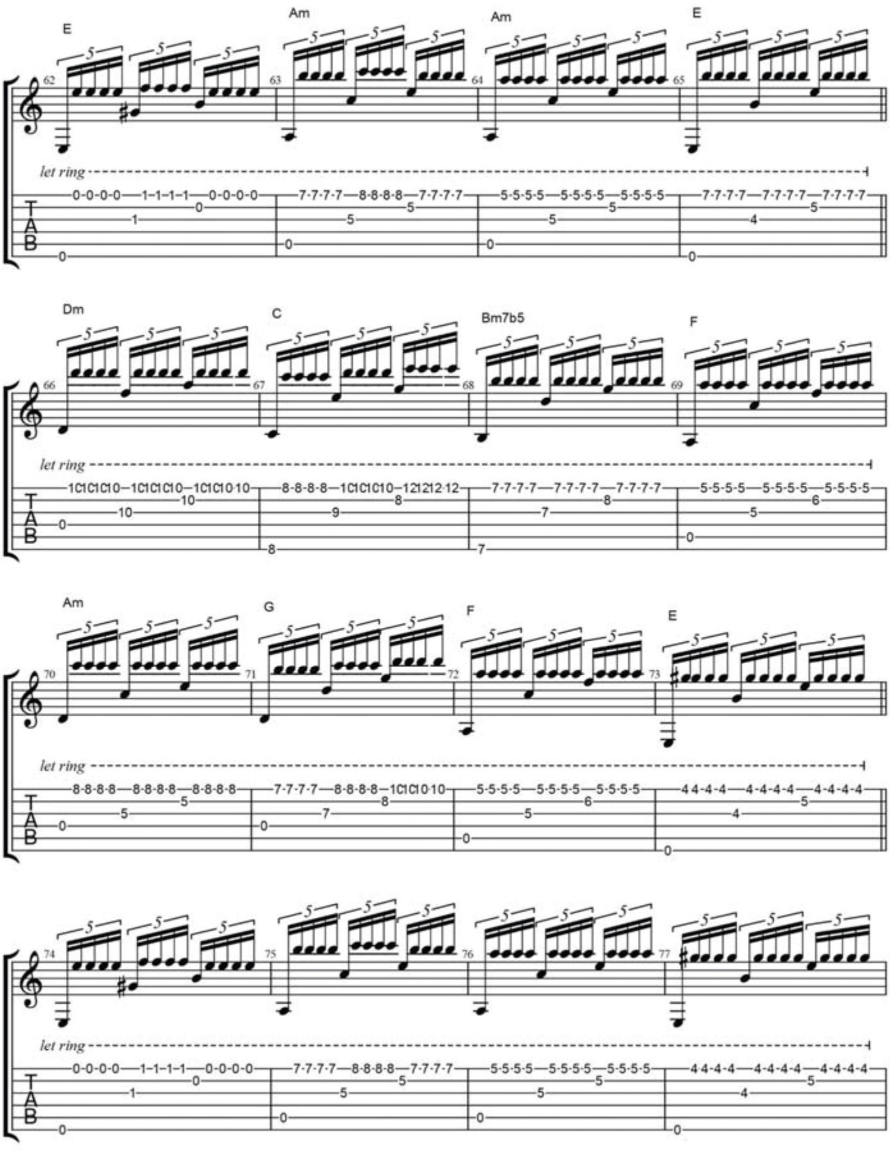
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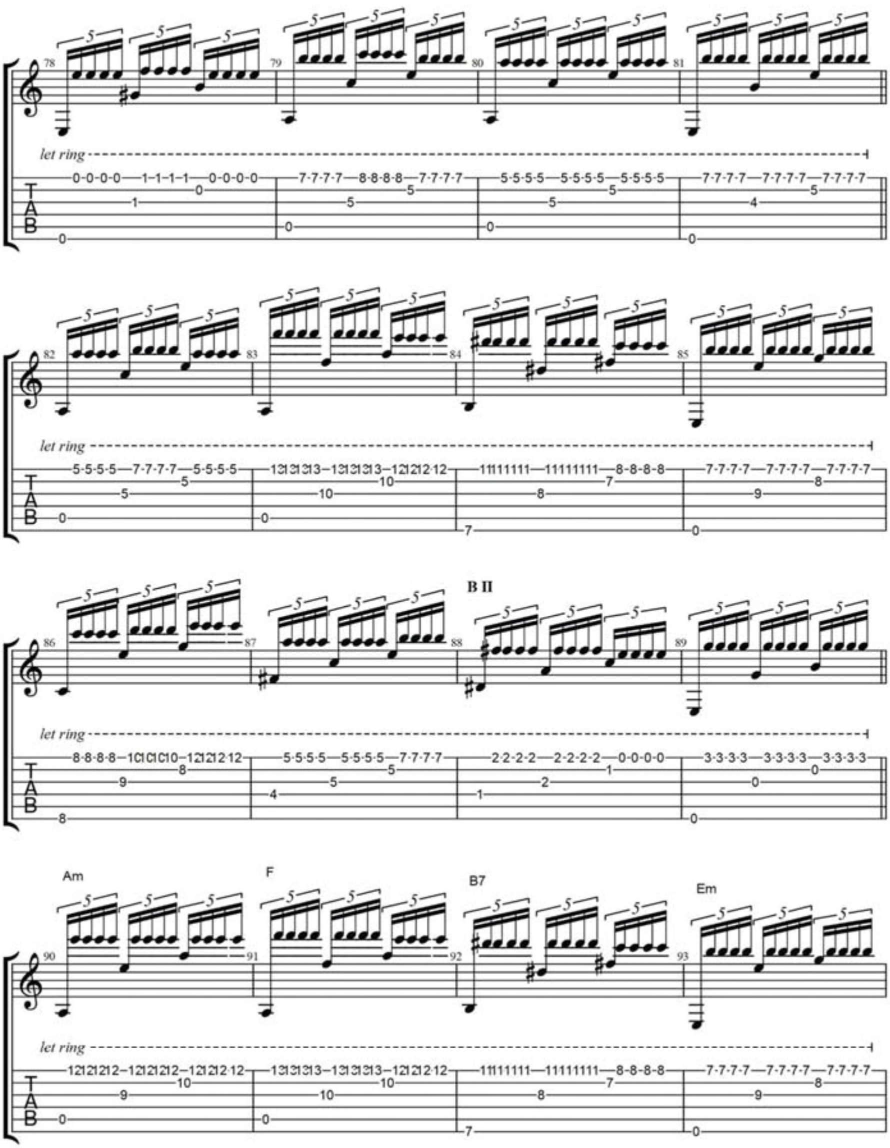
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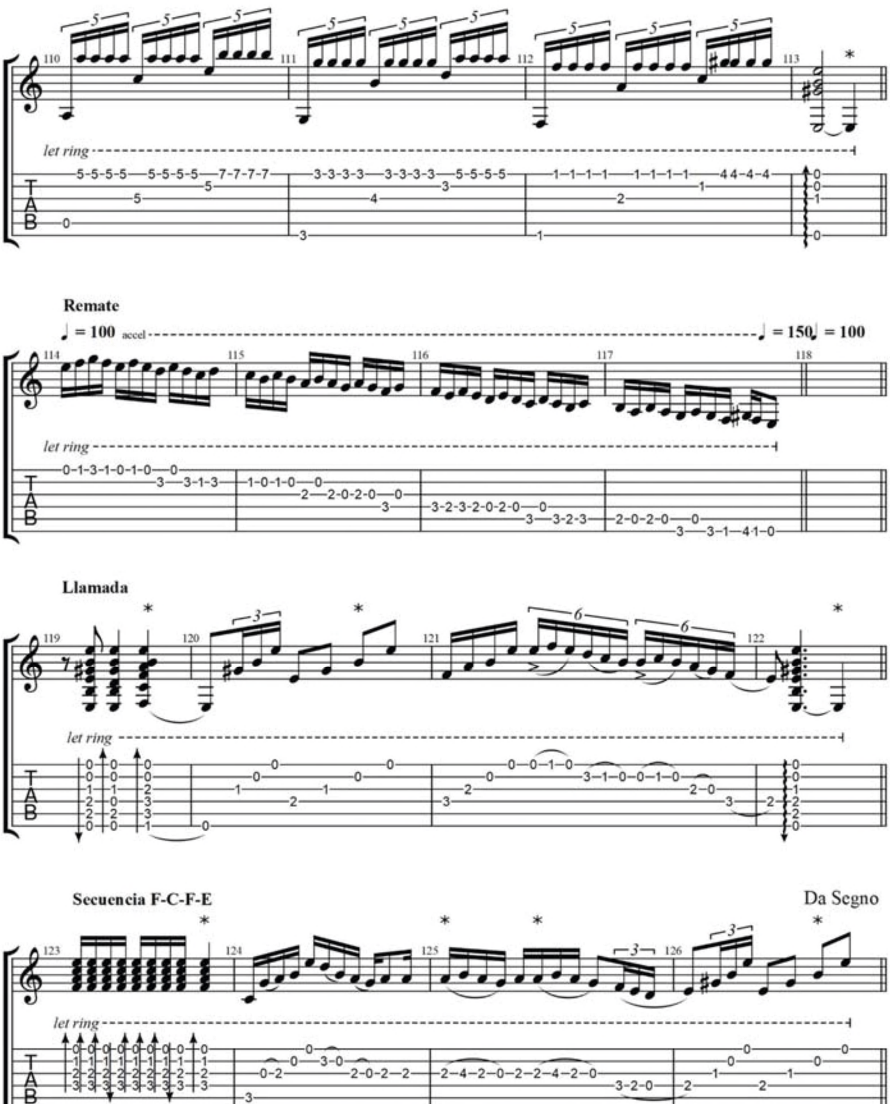
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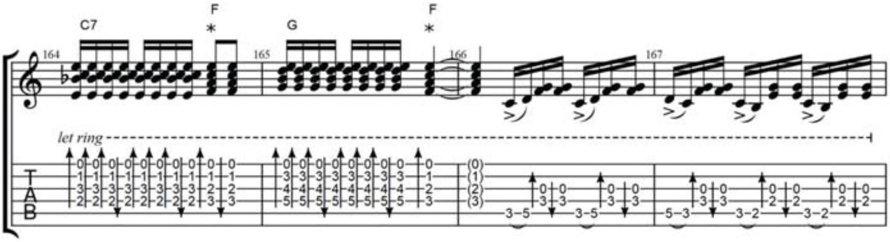

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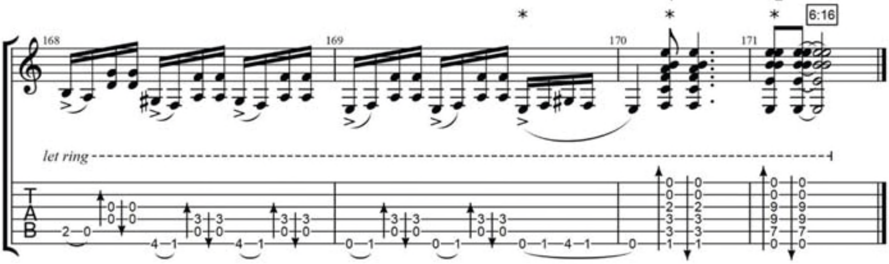

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