Jimma University

Jimma Institute of Technology

School of Biomedical Engineering

Bioinstrumentation Engineering stream

Analysing the Effects of Khat and Khat Addiction Rehabilitation Therapy on Heart Activity

A research report submitted to the School of Graduate Studies of Jimma Institute of Technology, Jimma University, in Partial Fulfilment for the Degree of Master of Science in Biomedical Engineering (Bioinstrumentation).

By: Ewunate Assaye

3rd March 2022

Jimma, Ethiopia

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Advisors

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3rd March 2022

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Declaration

I declare this research report with the title of "**Analysing the Effects of Khat and Khat Addiction Rehabilitation Therapy on Heart Activity**" as my original work and I assure it with my signature.

Ewunate Assaye Kassaw Signature---------------------------- Date: -----------------------

On behalf of the School of Biomedical Engineering at Jimma University, Jimma Institute of Technology we the advisors, the evaluators, and the chairperson of this research confirm that the report entitled "**Analysing the Effects of Khat and Khat Addiction Rehabilitation Therapy on Heart Activity**" is approved as MSc. thesis for the student.

Advisors

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2. Co-Advisor: Genet Tadesse (MSc.) Signature----------------------------- Date---17/04/22---

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Chairperson

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Abstract

Khat is a flowering plant whose leaves and stems are chewed for excitement purposes. It is very common in east African and Arabian countries. Khat can cause mood changes, increased alertness, hyperactivity, anxiety, elevated blood pressure, and heart diseases. However, the effect of khat on the heart has not been studied exclusively. The purpose of this study was to investigate the effect of khat chewing and rehabilitation therapy for khat addiction on heart activity.

ECG signals were recorded from 50 subjects (25 chewers and 25 controls) before and after chewing session to investigate the effect of khat on heart activity. In addition, ECG signals from 5 subjects were recorded in the first and eighth day of rehabilitation therapy for investigating the effect of rehabilitation therapy for khat addiction. All the collected signals were annotated, denoised, features extracted and analysed.

After chewing khat, the average heart rate of the chewers was increased by 4.82%, with 3 subjects out of 25 were prone to tachycardia. 1.39% QRS duration and 20.07% R-peak amplitude reduction were observed after chewing session. Moreover, heart rate variability was reduced by 18.24% indicating the effect of khat on suppressing sympathetic and parasympathetic nerve actions. After rehabilitation therapy, the average heart rate was reduced by 11.66%, while heart rate variability (HRV), QRS duration, and RR interval were increased by 25.43%, 3.49%, and 12.53%, respectively.

The findings demonstrate that, khat chewing raises heart rate, lowers heart rate variability, or puts the heart under stress by lowering R-peak amplitude and QRS duration, which in turn increases the risk of premature ventricular contraction, arrhythmia, and heart failure. The results also show that rehabilitation therapy from khat addiction has a major impact on restoring cardiac activity to normal levels.

Key Words: - Addiction, ECG, Feature Extraction, Heart disease, Heart rate, Khat, Rehabilitation.

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Abbreviations

AV - Atrioventricular

CT - Computerized tomography

CVDs – Cardiovascular diseases

CVS – Cardiovascular system

ECG - Electrocardiogram

ETB - Ethiopian birr

FEF - Expiratory flow rate

FEV1% - Flow rate in the first one second

FVC - Forced vital capacity

FVC1 - Forced vital capacity in one second

LA - Left arm

LL - Left leg

MRI - Magnetic resonance imaging

PEFR - Peak expiratory flow rate

RA - Right arm

RL - Right leg

SA - Sino-Atrial

VCIN - Inspiratory vital capacity

WHO – World Health Organization

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Chapter One

1. Introduction

1.1. Background

Khat is a flowering plant whose stems and leaves are chewed for recreational and stimulant purposes [1–3]. Khat leaves and buds have a mild aroma, astringent, and faintly sweet taste [3]. It elevates mood and produces euphoria [1–3]. It contains chemicals called cathinone and cathine which produce stimulant effects [3]. It can be preserved by wrapping it in banana leaves [1, 3]. Most commonly it is used by populations in East Africa and Arabia [1–3]. It is regularly consumed by about 20 million people [4–6]. It is illegal in the USA and Canada [1]. Khat is listed as one of the drugs that create dependence (a containing desire to keep using it) in people by WHO [1, 3]. Khat is becoming an emerging threat to the cardiovascular system in the United Kingdom [5]. Chewing increases the level of cathinone and amphetamine-like substances in plasma that increases blood pressure to cause hypertension [7–10]. It significantly affects the lung function indices, vital signs, and the cardiovascular system by affecting heart rate and blood pressure [7–12].

The effect of khat varies across people and it depends on the amount of consumption, time, as well as health, weight, and size of the person [3]. Talkativeness, faster heartbeat, faster breathing, increased blood pressure, hallucination, impaired judgments, paranoia, increased temperature, reduced appetite, decreased sexual desire, improved ability to study, aggression, alertness, improved concentration, feeling energetic and social are the short term effects [2, 3, 12–17]. Tachycardia, myocardial infarction, arrhythmia, heart attack, stroke, coronary artery diseases, liver diseases, fertility problems, digestive problems, sleep-related issues, seizure, mental health problems, schizophrenia and psychological dependence are some of the long term effects [3, 10, 12, 13, 15–20].

The main reasons for chewing khat are its social habit and it improves concentration while studying or working [8, 9, 21]. Associated factors of khat chewing include: being male, urban in residence, age group between 19 and 23 years, peer influence, family history of chewing khat, richest wealth quintiles, and alcohol drinking. Cigarette smoking, increased workload, and religious practice were also found to be independent predictors of chewing [21, 22]. 16% of all Ethiopian chew khat to an extent which can have a negative health impact [23]. In the previous two decades in Ethiopia, khat has surpassed coffee and oilseed as a key export crop in terms of output [24, 25]. Many coffee growers are switching to khat, as the khat trade is growing [24]. On average 100 grams of khat per individual is consumed in one day [26]. Withdrawal of khat may have symptoms like tiredness, lower blood pressure, and mild depression. The most common adverse effect is reported to occur on the cardiovascular system [27].

1.2. The cardiovascular system

The cardiovascular system (CVS) is a system that consists of the heart, the blood vessels, and blood. The heart is a muscular tissue responsible for pumping blood. Blood vessels are closed systems of vessels called arteries, veins, and capillaries. Blood is about 5 liters of fluid containing blood cells, nutrients, oxygen, carbon dioxide and water [28, 29]. CVS has three main parts of circulation systems. These are the part of circulation that takes blood from the heart to the whole body called systemic circulation, the part of the circulation that takes blood to the heart muscle called coronary circulation, and the part of circulation that takes blood to the lung called the pulmonary circulation [28], 29]. Figure 1.1 illustrates the overview of the cardiovascular system. It can also be thought of as a transport system in the body [28].

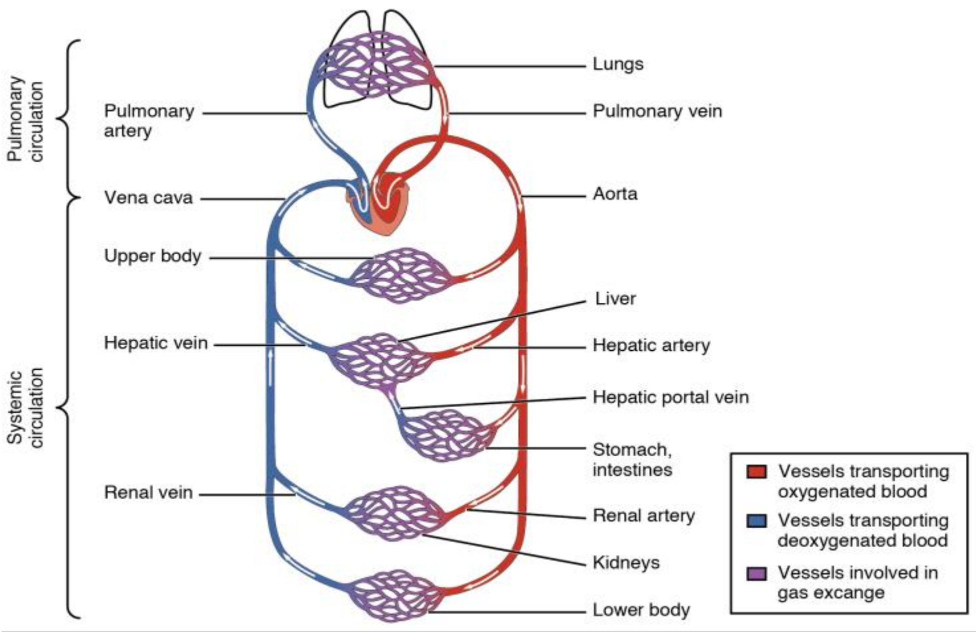


Figure 1.1 Overview of the cardiovascular system [28]

1.2.1. The Heart

The central organ of the cardiovascular system called heart is a cone-shaped organ with a size of a fist located at the centre of the thorax between the lungs directly behind the sternum breastbone [30]. It is a muscular pump tissue that pumps oxygenated blood to the whole-body tissues then collects the deoxygenated blood from the tissues to pump it to the lungs and receives the oxygenated blood back [30]. The heart regularly contracts and relaxes to force blood to flow to the circulatory system [28].

1.2.1.1. Anatomy of the heart

The heart is covered by a sac-like protective membrane called the pericardium. Pericardium secretes a fluid to reduce friction while the heart beats. The walls of the heart are made up of three layers. These are the outer layer called the epicardium, the middle layer made up of the cardiac muscle called myocardium, and the inner layer called the endocardium [30] as shown in Figure 1.2.

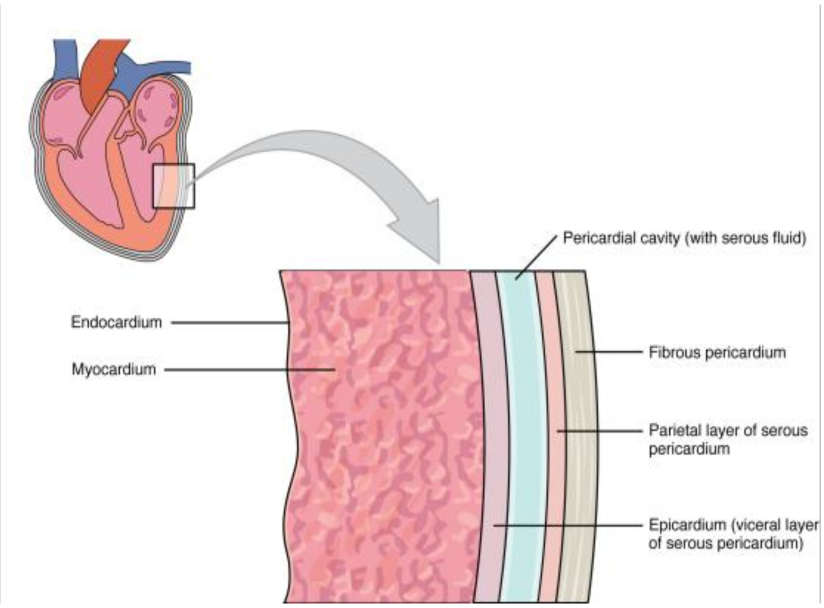


Figure 1.2 Layers of the heart wall [28]

The intercalated disks contained in the cardiac muscle cells enable the cells to communicate and allow direct transmission of electrical impulses in between. The cardiac muscle is not under the control of the conscious nervous system, it can generate its electrical rhythm at the sinoatrial node [28, 30, 31]. Cardiac muscles cannot get tired because they cannot respire anaerobically. The heart itself is supplied with oxygenated blood by the coronary artery. The heart beats over 2.5 million times in the average life span of a human being [28, 30, 31].

The heart has four chambers, these are the left ventricle, the right ventricle, the left atrium, and the right atrium. It also has four valves namely the aortic valve, mitral valve, pulmonary valve, and tricuspid valve. The aortic valve helps to prevent the backflow of blood to the left ventricle once it is pumped out. Mitral valve is located between the left atrium and the left ventricle to prevent the backflow of blood from the left ventricle to the left atrium. The pulmonary valve prevents the backflow of blood from the pulmonary artery to the right ventricle and the tricuspid valve prevents the backflow of blood from the right ventricle to the right atrium [28, 30, 31]. Figure 1.3 illustrates the four chambers and the four valves of the heart.

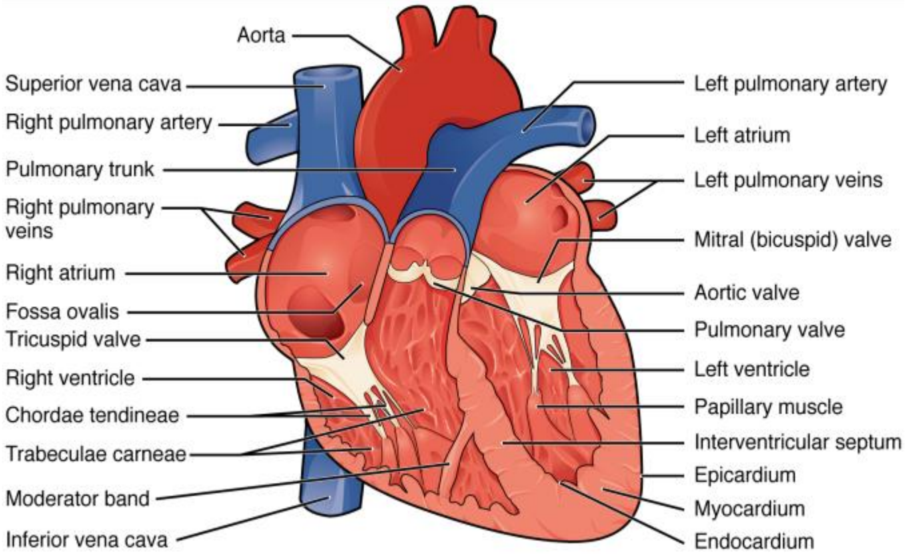


Figure 1.3 Anatomy of heart valves and chambers [28]

1.2.1.2. Physiology of the heart

The right atrium receives deoxygenated blood from the systemic and coronary circulation and pumps it to the right ventricle. The right ventricle receives deoxygenated blood from the right atrium and pumps it to the pulmonary circulation [28, 30, 31]. The thickest walled left ventricle receives oxygenated blood from the left atrium and pumps it to the systemic circulation and the coronary circulation. The left atrium receives oxygenated blood from the pulmonary circulation and pumps it to the left ventricle [28, 30, 31]. This pumping and receiving of blood create a sequential event of systolic and diastolic phases. While diastole the ventricles relax and fills blood. During the systolic phase, the ventricles contract, and blood is pumped out [28, 30, 31]. This sequence is termed as cardiac cycle. Figure 1.4 demonstrates the cardiac cycle.

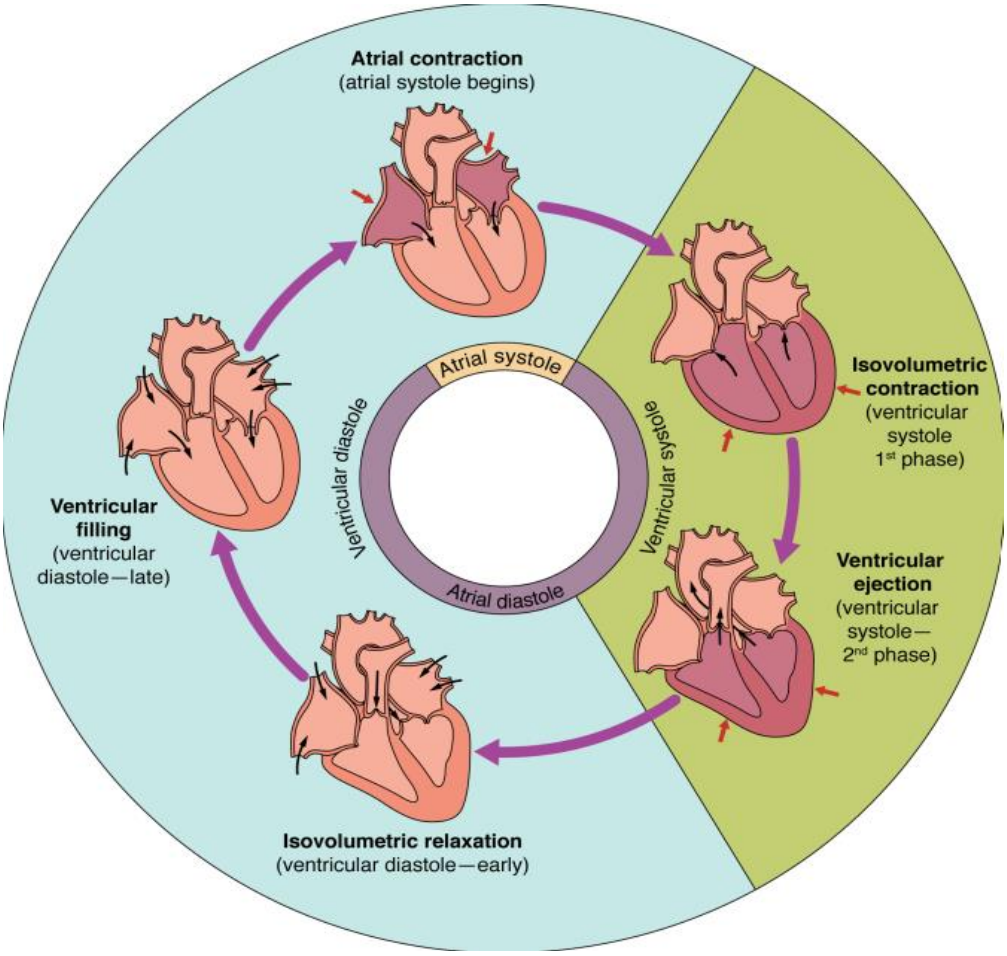


Figure 1.4 The cardiac cycle overview [28]

The heart has a specialized type of tissue called a node that behaves both as nervous and muscular tissue which are responsible for the contraction of the heart chambers. The heart has two nodes these are the sinoatrial (SA) node and the atrioventricular (AV) node. The SA node is the pacemaker of the heart located at the right atrium upper wall which coordinates the heart contractions. It generates the nerve impulses that travel throughout the heart wall to cause right and left atrial contraction. SA node is regulated by parasympathetic and sympathetic autonomic nervous systems to slow down and accelerate the heart rate respectively [28, 30, 31].

The AV node is located at the left bottom of the right atrium which delays the signal sent by the SA node about a tenth of seconds. This delay allows the atria to contract and pump blood before the ventricle starts to contract. After the delay, the AV node sends the signal down to the atrioventricular bundle and ventricles. The atrioventricular bundle also called a bundle of His is a bundle of cardiac muscle fibers that extends from the AV node to the septum of the heart. It splits into two bundles near the top of the ventricles and each bundle branch continues down to carry impulses to the left and the right ventricles [28, 30, 31].

Beneath the endocardium, there are specialized fiber branches called Purkinje fibers which are extended from atrioventricular bundle branches that rapidly relay the cardiac impulses to the myocardium cause the contraction of the ventricles. The myocardium is the thickest layer of the heart in ventricles and enables the ventricles to generate enough power to pump blood [28, 30, 31]. Figure 1.5 shows the cardiac muscle excitation sequence.

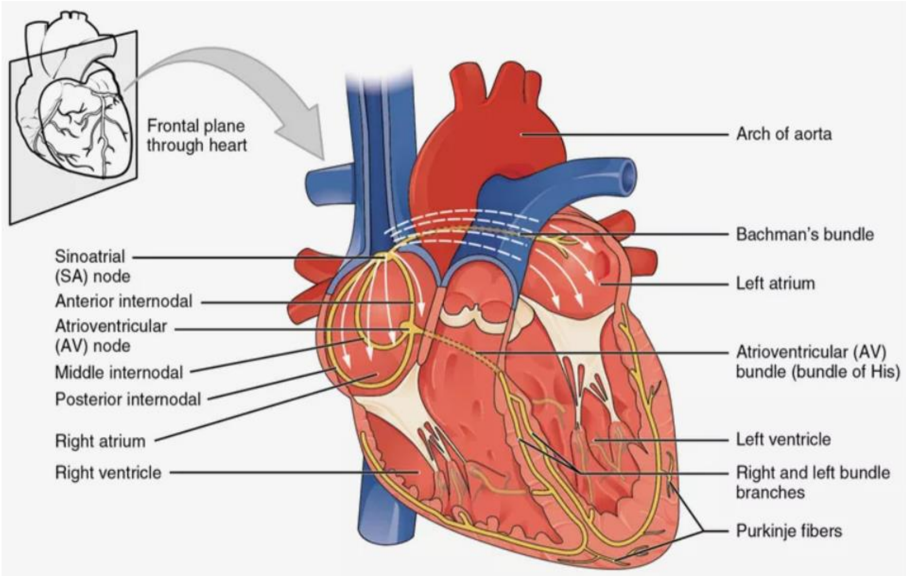


Figure 1.5 Excitation stages of the cardiac muscle [28]

1.3. Diagnosis methods of cardiac diseases

Starting from the physical and stethoscope examination, heart diseases can be diagnosed using different imaging modalities and laboratory tests. Blood tests, N-terminal and pro-B-type natriuretic peptide chemicals can be used to identify the signs of heart diseases. It is also common to use cardiac computerized tomography (CT) scan to collect the images of the heart and the chest from a different direction. Similarly, to get a physiological image of the heart cardiac magnetic resonance imaging (CMRI) can be used [32]. The conditions of the heart and other signs that indicate heart diseases can be observed from the chest X-ray. A thin flexible catheter can be inserted into the blood vessel (this method is called angiogram) at the groin or arm and guided to the coronary arteries to inject a dye for getting a visible X-ray image [32].

To test the types of heart muscle diseases a small piece of the heart muscle can be taken via a thin small flexible biopsy cord inserted into a vein through the neck or groin. From an echocardiogram image or video created using sound waves, it is possible to see the abnormalities related to shape, size, ejection fraction, and pumping status [32]. A stress test is another method of diagnosing the heart's status by applying certain stress such as walking on a treadmill, taking drugs, and wearing a mask to record the cardiac activity using ECG machine. ECG is the most common and affordable method to diagnose a variety of heart abnormalities by recording the electrical activity of the heart [32].

1.3.1. ECG representation

An electrocardiogram (ECG) is the graphical representation of the contractile electrical activity of the heart that helps to diagnose heart diseases from its main features [33]. The main features of the ECG are: - P wave, QRS duration, PR interval, Q wave, R wave, S wave, ST segment, P wave, T wave, QT interval, RR interval and heart rate [28, 30].

The P wave represents the depolarization of the atria. For a healthy person P wave exists preceding each QRS complex. PR interval represents the time taken by the electrical activity to move from the atria to the ventricle which starts at the starting of the P wave and ends at the beginning of the Q wave [28, 29]. The QRS complex represents the depolarization of the ventricles which is the interconnection of three closely related waves Q, R, and S. ST-segment represents the time between depolarization and repolarization of the ventricles. It starts at the end of the S wave and ends at the beginning of the T wave. T wave represents the ventricular repolarization and appears as a small wave after the QRS complex [28, 29]. RR interval represents the time between two QRS complexes. It starts at the peak of one R wave and ends at the peak of the next R wave. QT interval represents the time taken by the ventricles to depolarize and then repolarize. It starts at the beginning of the QRS complex and ends at the end of the T wave [28, 29]. Figure 1.6 demonstrates the important features of the ECG signal.

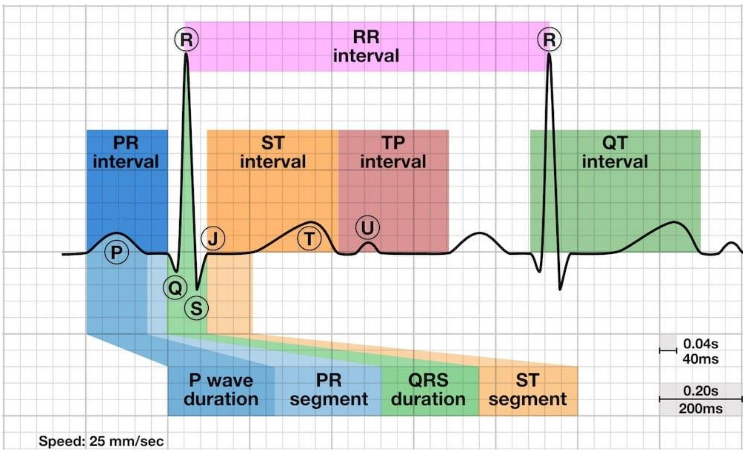


Figure 1.6 The features of Electrocardiogram [34]

1.4. The effect of addictive drugs on the cardiovascular system

Cardiovascular diseases (CVDs) are the number one killer in Europe, United States, and globally [35–37]. It kills more people annually than any other disease [36, 37]. In 2000 39% of deaths in the united states were due to CVDs [36, 37]. In 2010, 29.6% of global deaths were due to CVDs [35]. In 2015 about 17.9 million people died from cardiovascular disease which is 31% of total global death [38]. In Ethiopia the prevalence of cardiovascular disease is about 24% [39].

Addictive drug consumption can have adverse cardiovascular effects including arrhythmia and heart attack [40]. Addictive drugs such as alcohol and nicotine have the effect of altering the electrophysiological properties of the heart and causing arrhythmia [41, 42]. Even though alcohol has the advantage of protecting a person from stroke and coronary artery diseases, abusive usage can cause chronic arrhythmia, hypertension, and cardiomyopathy [43]. Tobacco consumption increases the risk of vascular diseases, heart attacks, and stroke [44, 45]. Electronic cigarettes may substantially increase the risks of cardiovascular, noncancer lung diseases, asthma, bronchitis, emphysema, and chronic obstructive pulmonary diseases: which accounts more than half of all the smoking-induced deaths by exposing the users to a high level of ultrafine particles and toxins [41].

Consumption of marijuana delivers harmful substances and cannabinoids to the body, which can pose risks such as arrhythmia, myocardial infarction, cardiomyopathy, cardiac arrest, stroke, and faster heartbeat [46, 47]. Usage of marijuana has a risk of causing bronchitis, cough, phlegm secretion, scarring, and damage to the blood vessels of the lung [48]. Amphetamine causes acute and chronic cardiovascular diseases from its toxicities [43]. Arrhythmia, pulmonary oedema, and reduced cardiac output can result from heroin and other opiate consumption [43]. Cardiovascular problems such as bacterial infection of the heart valves, the collapse of veins, and infection of blood vessels can result from injection drug usage [49, 50].

Chronic cocaine consumption has well recognized and significant toxic effects such as potassium and sodium channel blockade, mitochondrial damage, oxidative stress, and sympathomimetic effects on the heart. It has also a risk of deterioration or inflammation of the heart muscle, aortic ruptures, and the effect of reducing blood flow to the gastrointestinal tract [51]. Chest pain resulted from cocaine use is associated with CVDs such as arrhythmia, myocardial infarction, coronary atherosclerosis, acute hypertension, cardiomyopathy, myocardial ischemia, and endocarditis [51, 52]. Cannabis use was causing the occurrence of arrhythmia, myocardial infarction, heart failure, coronary artery disease, sudden cardiac death, tachycardia, cerebrovascular accident, and hypertension [53, 54].

The most used addictive drug in Ethiopia is khat [55]. Khat consumption causes blood pressure elevation and cardiac abnormalities [8–10, 56–59]. As studies have shown, coffee and tea have a stimulating and hypertensive effect with excessive dosage which leads to arrhythmic and cardiac abnormality stages [60, 61]. Coca-Cola, sprite, and other related soft drinks may damage the cardiovascular system due to their caffeinated or high sugar level behaviours [62, 63].

1.5. Problem statement

Cardiovascular diseases (CVDs) are the number one killer non-communicable disease in Ethiopia and worldwide. Moreover, the prevalence of cardiovascular diseases is increasing through time due to the adaption of sedentary life styles. Lack of physical exercise, unhealthy diet, smoking, obesity, diabetics, alcohol, cocaine, cannabis, marijuana, opium, and medications for other diseases are some of the possible causes of cardiovascular diseases.

Studies shows that khat is one of the drugs whose most common adverse effect is reported to occur on the cardiovascular system. Despite this, chewing becomes a habit among many youths in Ethiopia for its stimulation and euphoric effect. Many Ethiopians chew khat to an extent which can have a negative health impact.

Even though studies had been conducted on the effect of khat on heart, none of them had studied the exclusive effect of khat by controlling other drugs and drinks mostly taken with it. The previous studies were conducted without considering the effects of caffeinated drinks taken while chewing and using khat extracts instead of fresh khat leaves. For these reasons, it is difficult to say the abnormal effects reported are exclusively due to khat use.

In Ethiopia the vulnerability to khat addiction is increasing but the impact of rehabilitation therapy on khat addicts' heart activity is not investigated.

1.6. Objective

1.6.1. General objective

The general objective of this study is to investigate the effect of khat and khat addiction rehabilitation therapy on heart activity.

1.6.2. Specific objective

The specific objectives of this study are

- ✓ To detect the effect of khat chewing on heart activity.
- ✓ To detect the effects of rehabilitation therapy on khat addict’s heart activity.

1.7. Hypothesis

Khat chewing harms the heart activity by causing premature ventricular contraction, arrhythmia, and cardiac failure. These abnormalities can be restored by proper rehabilitation therapy.

1.8. Significance of the study

The findings of this study will be helpful to the health sectors for teaching the community about the adverse health effect of khat chewing. It will be used as an input for expanding and establishing rehabilitation therapy centres. Researchers will use this research for studying further on the issue.

1.9. Scope of the study

The scope of this study will be limited to collecting ECG data from healthy non-chewers, healthy chewers, and an addicted subject, pre-processing the collected data, extracting features, and analysing the results. The ingredients of khat, blood pressure, temperature, physical examination results, and other unmentioned issues are not within the scope of this study.

Chapter Two

2. Literature Review

A study conducted in Yemen between the years 1997 and 1999 showed that khat chewing significantly increases the risk of acute myocardial infraction for heavy chewers up to 39-fold compared to nonchewers [8]. Analysis of the collected data from 1200 (600 chewers and 600 non-chewers) voluntary individuals through interview and physical measurement in a regular time interval of 7:00 am to 10:00 am, using linear regression and binary logistic regression has proved that the mean value of diastolic and systolic blood pressure was significantly higher in chewers [9].

According to the research conducted in Ethiopia from selected 60 persons, with an average chewing rate of 200 grams of fresh "Beleche" 1.7 times per week khat has a significant effect on inspiratory vital capacity (VCIN), forced vital capacity (FVC), forced vital capacity in one second (FVC1), the flow rate in the first one second (FEV1%), expiratory flow rate (FEF) and peak expiratory flow rate (PEFR) [10]. Additionally, the ventricular depolarization and conduction velocity increased by 11%, the R-R interval reduced by 9%, and the QT interval reduced by 4.5% [10]. Thirty cardiac patients and thirty normal subjects were selected and non-sustained ventricular tachycardia was found on 7(23.3%) of the thirty cardiac patients during khat chewing day and only on 2 (6.6%) on khat-free days [56]. For the healthy groups, 1(3.3%) person showed short runs of ventricular tachycardia on khat chewing day and no ventricular tachycardia on khat-free days [56].

A study done on 422 male chewers has been proved that frequent chewers have fourteen times more possibility of elevated systolic blood pressure compared to less frequent chewers [57]. Khat chewers were more likely to have an elevated ST segment, higher risk of myocardial ischemia, cardiogenic shock, ventricular arrhythmia, and stroke compared with nonchewers [58]. Khat chewing was associated with the risk of an acute coronary syndrome, increased the risk of stroke and death [59]. For pregnant women chewing induces chest pain, tachycardia, and hypertension [64]. Using a community-based cross-sectional study in Nekemte town the collected data from 359 individuals shows that the risk of anxiety was five times more in chewers and the risk of depression was 25 times higher in chewers when compared to nonchewers [65]. According to the qualitative research done on 37 Somali community members and 11 primary caregivers chewing leads to the occurrence of adverse physical and mental effects, neglecting social responsibility, social isolation, and family breakdown [66].

The study conducted on 20,434 youths in school and out of school showed that daily khat chewing has an association with unprotected sex [67].

The studies conducted on the area of khat effects on the cardiac activity can be grouped into three categories based on their methodology. In the first category, the studies were conducted on humans or rats by using the extracts of khat that cannot fully represent the fresh khat chewed by most subjects. While extracting khat there is a possibility of losing constituents, evaporating components, and aroma. In the second category, the studies were conducted on cardiovascular patients. There is a possibility of many other determining factors together with khat to induce the existing abnormality. In the third category, the studies were conducted on healthy subjects without controlling the usage of cigarettes, coffee, tea, Coca-Cola, sprite, and other caffeinated or high sugar level beverages those have their own effect on the heart activity.

Even though cardiovascular disease is very fatal it can be prevented by addressing behavioural risk factors such as addictive drug consumption, unhealthy diet, alcohol use, obesity, and physical inactivity [36, 37]. The health condition of 47 people rehabilitated from khat addiction in Saudi Arabia showed that quitting khat improved their health dramatically [68]. All of the participants were rehabilitated and began a better life than they had before their khat addiction [68]. The results of a study conducted on 855 addicted people in Canada from April 18 to June 1 2016 revealed that rehabilitation therapy considerably improved health status and life quality [69]. According to a study conducted on 34 opium-addicted individuals, adding physical activity as a rehabilitation therapy was extremely beneficial in regaining a normal heart rate and blood serotonin and dopamine levels [70].

Chapter Three

3. Methodology and Materials

3.1. Methodology

To study the exclusive effect of khat and khat addiction rehabilitation therapy chewer subjects, control subjects and khat addicted subjects admitted to the rehabilitation centre were selected. The variations in ECG signal features were retrieved using signal processing techniques to analyse the changes in cardiac activity. Figure 3.1 shows the general procedure used in this study.

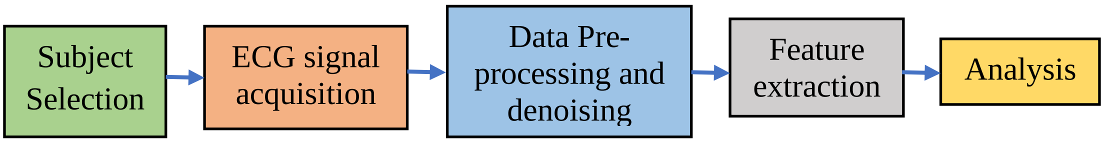


Figure 3.1 General procedure of the study

3.1.1. Study area

Data collection of healthy control and chewer subject's ECG signal was conducted in Jimma town located 352 kilometres from the capital city of Ethiopia, Addis Abeba. The ECG signal data of khat addicted subjects before and after rehabilitation therapy was collected at Saint Paul's Hospital Millennium Medical College in Addis Abeba.

3.1.2. Ethical approval and informed consent

Institutional Review Boards of Jimma institute of health, Jimma university, with permission number JHRPGN/75/21, and Institutional Review Boards of Saint Paul's hospital millennium medical college, with approval number pm23/385, provided ethical approval letters for the study to be conducted. Prior to data collection, all participants signed an informed written consent form.

3.2. Subject selection

The study's participants were chosen based on the selection criteria that needed to be met. To reduce the impacts on heart activity, factors with possibility of affecting heart activity such as coffee, alcohol, cigarette, and another addictive drug usage were prohibited. The next sections go over the selection criteria in further detail.

The effect of khat on heart activity: - The recruited subjects were chosen using a pilot sampling strategy for this portion of the study. The subject selection criteria for investigating the effect of khat on heart activity were: -

1. Voluntary: - able to comply to the study's restrictions and conditions, such as abstain from chewing khat [71] and drinking alcohol for at least two days, drinking coffee for the last 12 hours, soft drinks for the last 8 hours, and tea for the last 6 hours prior to data collection.
2. Young adults: - between the ages of 20 and 30.
3. Healthy: - did not have any confirmed case of cardiovascular diseases and is not taking any medicine that affects heart activity.
4. Free from any addictive drug use such as cocaine, marijuana, cannabis, and cigarette.

A non-chewer control subjects were selected for every selected chewer subject (chewer and control subjects matched) based on sex, age, and body mass index (BMI). Each subject should provide a pair of ECG signals before and after the chewing session for the data to be complete. Before any recording, all the subjects were instructed to have their lunch. Individuals chewed an average 100 grams of khat [26]. 100 grams of the same type of khat was given to each khat chewer subject. This research utilized Kellechaa khat, which is the most widely available, preferred, and consumed khat in Jimma town. Kellechaa is a popular khat type grown in Medabuna rural area east of Jimma town. During the chewing session, tea, coffee, Coca-Cola, Sprite, and cigarette smoking were prohibited. Since khat is bitter to chew it alone peanuts were used.

Rehabilitation therapy from khat addiction: - ECG signal data was obtained from khat addicts admitted to Saint Paul's Hospital Millennium Medical College to investigate the effect of rehabilitation therapy. In this portion of the research case study approach was used. Subjects were excluded from the study due to addictions to other drugs such as alcohol, cigarettes, marijuana, opium, or a combination of one or more of these. For this study, the participant would take the medicines such as benzodiazepine, antidepressant or clonidine and therapies like watching TV, playing dart, playing table tennis, weight lifting, rope jumping or other sport activities as recommended by the physician.

3.3. ECG signal acquisition

The ECG signal from the selected subjects was recorded using lead II. As it's parallel to the heart's depolarization path, lead II is most usually used and preferred for monitoring cardiac activity. it allows a clear visualization of the ECG signal PQRST waveform, intervals, and segments [72]. The participants were in a conventional ECG recording sitting position when the signal was recorded. The participants were sat in a steady position to reduce any noises from muscle movement and respiratory muscle artefacts.

3.3.1. ECG Recording

Each individual had taken a 5-minute seat rest to reduce the impact of any potential physical movements. The ECG signals of matched chewer and control participants were recorded sequentially to account for environmental influences that may alter heart activity.

Participants in this study underwent an ECG signal recording procedure as outlined in the Biopac student lab lesson five Electrocardiography (ECG) measurement manual. Near the electrode placement areas, watches and jewellery were removed. Alcohol was used to clean the electrode attachment site's skin. The subjects were seated upright and relaxed prior to recording. The leads were placed using typical lead II configuration. The negative electrode was placed on the side of the palm of the right forearm above the wrist, the positive electrode on the interior left leg just above the ankle, and the reference electrode on the interior right leg just above the ankle [73]. The electrodes positioned on the skin 5 minutes before calibration were done to increase skin-electrode contact. Then the subject's pre-chewing ECG signal was recorded for 1 minute.

For the post-chewing session recording, Kellechaa khat was purchased based on the number of chewers for the day. Khat leaves were prepared by removing any non-chewable components. Each chewer was given 100 grams of khat leaves, two litters of water and peanuts. The peak of excitement usually happens two hours after the initial chewing session [71]. Additionally, the chewers were able to pinpoint their highest excitation period. The ECG signals were recorded using the same procedure as the pre-chewing session. The ECG recording procedure is also the same for the effect of rehabilitation therapy on heart activity portion of the study. Figure 3.2 shows the ECG signal acquisition procedure for investigating the effect of khat on heart activity.

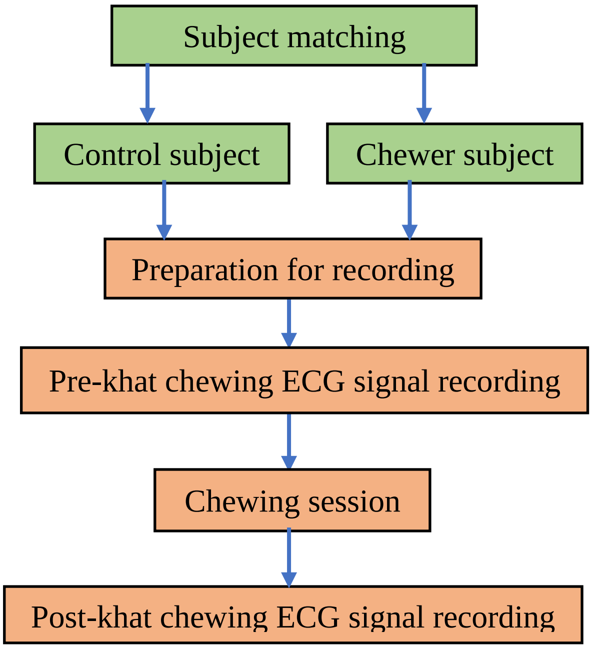


Figure 3.2 ECG data acquisition procedure to investigate the effect of khat on heart activity

The first recording for studying the effect of rehabilitation therapy from khat addiction on heart activity was done on the first day the individuals were admitted to the hospital. To reduce the effect of physical movement on ECG signal measurement, the individuals were given a 5-minute sitting rest. The rules and procedures were similar to the rules and procedures used for studying the effect of khat on the heart activity. The second recording was done on the eighth day of admission, using the same recording protocols as the first. Figure 3.3 shows the procedure used to collect the data for studying the effect of rehabilitation therapy from khat addiction on heart activity.

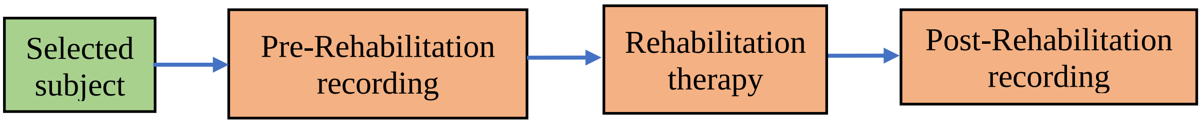


Figure 3.3 ECG data acquisition procedure to investigate the effect of rehabilitation therapy from khat addiction on heart activity

Figure 3.4 illustrates the overall setup and electrode placement pictures captured during the signal acquisition procedure.

Figure 3.4 Data recording and electrode setup.

3.3.2. Collected data

The effect of khat on heart activity: - A total of 100 ECG signals were obtained from 50 participants. 50 of the recorded ECG signals were collected before the chewing session and the remaining 50 signals recorded after chewing session. Out of those 50 healthy pre-chewing signals 25 of those were provided by the chewer subjects, and the remaining 25 by the control participants. The chewer subjects provided 25 signals out of the 50 post chewing signals, whereas the control individuals provided the remaining 25. Among the 50 individuals 38 of them were male, with 19 control and 19 chewer subjects; the remaining 12 were female, with 6 control and 6 chewer subjects. According to the collected information the lowest BMI value is 18.6 and the highest BMI value is 24. Adults with a BMI of less than 18.5 are considered underweight, those with a BMI of 18.5 to 24.9 are considered as normal, those with a BMI of 25.0 to 29.9 are considered as overweight, and those with a BMI of greater than 30 are considered as obese [74].

Rehabilitation therapy from khat addiction: - data was acquired from 5 khat addicted subjects admitted to Saint Paul's Hospital Millennium Medical College. The ECG signal was taken from those 5 participants prior to rehabilitative therapy. The ECG signal was also taken from those participants following a week of rehabilitation therapy on the eighth day. The health condition of the khat-addicted participants were recovered after a one-week stay in the rehabilitation program. To account for the potential effects of environmental changes on heart activity over time, the recording time was kept same throughout all recording days. For this study 10 ECG signals were recorded from khat addicted subjects. Out of 10 ECG signals 5 signals were recorded before rehabilitation therapy and 5 signals were recorded after rehabilitation therapy. Before rehabilitation, 1 of the 5 individuals was tachycardic. 4 of the 5 participants were men. The individuals were 23, 28, 31, 35, and 38 years old.

3.4. Signal Pre-processing

Following the recording procedure, signal annotation was performed. The recorded signals were given a unique name that identified the subject category, recording session, and counting number. Then the signal length was adjusted to 60 seconds. ECG signals are susceptible to disturbances such as baseline wandering abnormalities, powerline interference, EMG noise, and electromagnetic interference. As a result, any unwanted noises should be eliminated before extracting the relevant features. Baseline wandering noises are caused by respiratory muscle movement, temperature change, and electrode motion artefacts. The noise from respiratory muscle movement or electrode motion artifact has a frequency range of 0.3 to 0.6 Hz, and temperature variation noise has a frequency range of up to 0.1Hz [75]. Figure 3.5 shows the pre-processing and denoising procedure used in this study.

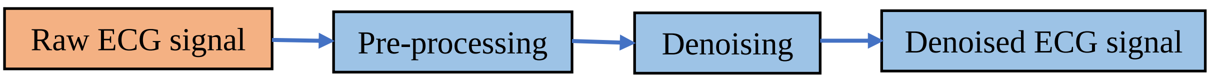


Figure 3.5 Pre-processing procedure of the study

3.4.1. Smoothing using Savitzky Golay filter

Savitzky Golay was employed to smooth the signal and remove low frequency disturbances. The Savitzky Golay method offers the advantage of maintaining the most significant characteristics of an ECG signal, such as relative maxima, minima, and width [76–80]. The least square polynomial regression approach is used in the Savitzky Golay finite impulse response filter [79]. To take the calculated central point of the fitted polynomial it takes the least-squares fit from consecutive small data set points [78, 79]. The mathematical description of the Savitzky Golay filter is given by Equation 3.1.

$$S_j^* = \frac{\sum_{i=-m}^{i=m} C_i S_{j+i}}{N} \quad \text{Eq. 3.1}$$

where S^* is the smoothed signal, C_i is the coefficient of ith smoothing, S is the original signal, m is the half-width of the smoothing window, j is the running index of the original data, and N=2m+1 is the number of data points in the smoothing window [80].

3.4.2. Denoising using discrete wavelet transform

Discrete wavelet transform provides great performance for denoising ECG signals [77, 81–83]. In the discrete wavelet transform (DWT), different cut-off frequencies are utilized to analyse the signal at different scales. A series of high pass filters were used to analyse high-frequency components, while a series of low pass filters were used to analyse low-frequency components. Using DWT, the discrete function f_n (the signal) is represented by Equation 3.2.

$$f_n = \frac{1}{\sqrt{M}} \sum_k w_\varphi(j_0, k)\varphi_{j_0,k}(n) + \frac{1}{\sqrt{M}} \sum_{j=j_0}^{\infty} \sum_k w_\psi(j,k)\psi_{j,k}(n) \quad \text{Eq. 3.2}$$

where $\frac{1}{\sqrt{M}} \sum_k w_\varphi(j_0, k)\varphi_{j_0,k}(n)$ is a weighted summation of scaling function ($\varphi(n)$) which is an approximation coefficient, $\frac{1}{\sqrt{M}} \sum_{j=j_0}^{\infty} \sum_k w_\psi(j,k)\psi_{j,k}(n)$ is a weighted summation of wavelets $\psi(n)$ which represents the detail coefficients, j_0 is an arbitrary starting scale, and n=1,2,3,…M.

Based on the signal to noise ratio (SNR), the best mother wavelet was chosen. SNR is the ratio of signal power to noise power. The higher the SNR indicates the lower contaminating noise power and cleaner signal. The lower the SNR indicates the higher noise power and heavily contaminated signal. Equation 3.3 is used to compute SNR [84].

$$SNR = \frac{signal\ power}{noise\ power} \quad \text{Eq. 3.3}$$

In decibel format SNR is represented by Equation 3.4.

$$SNR = 20\,log\frac{signal\ power}{noise\ power} \quad \text{Eq. 3.4}$$

The SNR values were calculated using Equation 3.4 throughout this research. The best suited mother wavelet was chosen from each family by computing the SNR value. Discrete Meyer (dmey) wavelet had scored the best SNR value as shown in Table 3.1.

Table 3.1 SNR values of different mother wavelets

Wavelet type	Signal to noise ratio value
bior3.9	69.06
bior4.4	75.50
bior6.8	75.84
coif4	75.97
coif5	75.96
dmey	80.64
db12	75.90
db13	75.94
db14	75.94
rbio1.5	74.79
rbio5.5	69.75
rbio6.8	75.88
sym12	75.94
sym13	75.94
sym14	75.91

A thresholding approach was necessary for wavelet denoising to select the amplitude of the signal to be approximated either to the lower or upper limit of magnitude. The two types of thresholding methods are hard and soft thresholding. In hard thresholding, if the absolute value of a wavelet coefficient is less than a particular threshold value, it must be set to zero; otherwise, the wavelet coefficient value remains unchanged [85]. For a given threshold value λ and a certain wavelet coefficient ω hard thresholding is given by Equation 3.5.

$$\omega = \begin{cases} \omega \ if \ \ |\omega| \geq \lambda \\ 0 \ if \ \ |\omega| < \lambda \end{cases} \qquad \text{...Eq. 3.5}$$

In soft thresholding, if an absolute value of a wavelet coefficient is less than a given threshold it will be set to zero; otherwise the threshold value will be subtracted from the absolute value of the wavelet coefficient and multiplied by the sign of the wavelet coefficient [85]. Mathematically soft thresholding is given by Equation 3.6.

$$\omega = \begin{cases} [sign(\omega)][|\omega| - \lambda] & if \ \ |\omega| \geq \lambda \\ 0 & if \ \ |\omega| < \lambda \end{cases} \quad \text{...Eq. 3.6}$$

It was confirmed that hard thresholding outperforms soft thresholding using SNR values. The SNR values of hard thresholding, soft thresholding, soft thresholding followed by hard thresholding, and hard thresholding followed by soft thresholding are presented in Table 3.2.

Table 3.2 SNR values of thresholding methods

Thresholding technique	Soft thresholding	Hard thresholding	Soft followed by hard thresholding	Hard followed by soft thresholding
SNR values	60.90901	68.30345	60.90901	68.30345

To determine the given threshold value λ fixed, heuristic, minimax, and rigorous are some of the thresholding techniques. The basic and general thresholding technique which enables to find the accurate information of the signal is universal thresholding also called sqtwolog thresholding given by the Equation 3.7 [86, 87].

$$\lambda = \sigma i\sqrt{2\,log(I)} \quad \text{...Eq. 3.7}$$

The variable σi is the standard deviation of noise and I is the number of samples. A global thresholding method that uses minimax method to find the threshold is minimax thresholding given by the Equation 3.8 [86, 87].

$$\lambda = \sigma i(0.3936 + 0.1829\,log_2 I) \quad \text{...Eq. 3.8}$$

Rigrsure thresholding is an impartial risk evaluator given by the Equation 3.9

$$\lambda = \sigma_i\sqrt{\omega_b} \quad \text{...Eq. 3.9}$$

ω_b is the square of bth wavelet coefficient. In case of poor signal condition heuristic thresholding can be used which is the combination of rigrsure and sqtwolog thresholding techniques [86, 87]. According to the calculated SNR value results in Table 3.3 heuristic thresholding method best suits for this study than others.

Table 3.3 SNR values of thresholding techniques

Thresholding method	Fixed thresholding	Heuristic thresholding	Minmax thresholding	Rigorous thresholding
SNR values	65.96371	75.77721	68.30345	71.92732

Finally, the wavelet coefficients were denoised using the selected parameters and the denoised coefficients were reconstructed.

3.4.3. Denoising using wavelet multi resolution analysis

There were some noises in the wavelet denoised signal. To eliminate the residual noise from the crucial signal, a different technique was required. A powerful technique for denoising noise-contaminated signals based on the frequency band and energy contribution of wavelet coefficients called signal multi resolution analysis was used.

By decomposing mono or multidimensional signals into "scaling" and "wavelet" functions, wavelet-based multiresolution analysis can be used for analysis, processing, and synthesis at many levels of resolution [88]. The multiresolution analysis idea provides a framework for signal decomposition in the form of a succession of decreasing-resolution approximations combined with a collection of details [88]. As a result, multiresolution analysis generates a family of orthonormal wavelets and eliminates redundancy [88].

Using the parameters selected in the previous section the wavelet denoised signal was decomposed into wavelet coefficients and the energy of each coefficient was computed. Additionally, the frequency band of each wavelet coefficient was specified, that was highly useful for determining which components should be included and discarded while reconstructing the signal. The energy of each coefficient is given by Equation 3.10.

$$E_j = log\left(\sum_{i=0}^{N}|coef(i)|^2\right) \quad \text{Eq. 3.10}$$

E_j is the energy of j^{th} layer detail coefficient, N is the number of detail coefficient of the j^{th} layer, coef(i) represents the j^{th} layer i^{th} detail coefficient [85].

As the signal's sampling frequency is 1000Hz, the wavelet decomposition has frequency range patterns of 250-500 Hz, 125-251 Hz, 62.4-125 Hz, 31.2-62.6 Hz, 15.6-31.3 Hz, 7.79-15.7 Hz, 3.9-7.83 Hz, 1.95-3.92 Hz, 0.975-1.96 Hz, 0.487-0.979 Hz, 0.244-0.489 Hz, 0.0-0.243Hz for detail (D) coefficients D1, D2, D3, D4, D5, D6, D7, D8, D9, D10, D11 and approximate (A) coefficient respectively. The low-frequency coefficients having a frequency range less than 1Hz had a great contribution to the overall signal energy (about 35.20 % in most cases) but their frequency was already out of the ECG signal range. Decomposition level 9 was the best choice for excluding frequency components with values less than 0.979Hz during reconstruction. Similarly, the coefficients in ECG frequency range with insignificant energy contribution need to be excluded during reconstruction. The powerline interference and EMG noises are expected to have frequency range greater than 30Hz which contributed about 0.85% of the total energy. So, it is acceptable to remove powerline and EMG noises by excluding the frequency range greater than 30Hz.As a result, for reconstructing the denoised signal the contributor coefficients were from level five to level nine as shown in Equation 3.11.

$$Denoised\ signal = Level5 + Level6 + Level7 + Level8 + Level9 \ldots\ldots\ldots \text{Eq. 3.11}$$

3.5. Feature extraction

Time domain features were the key ECG features utilized to examine the effect of khat and rehabilitation therapy on cardiac activity. The temporal peak detection and interval calculation techniques were used to calculate the time domain ECG characteristics, following the pan Tompkins QRS detection [89] approach. Figure 3.6 shows the feature extraction model employed in this study.

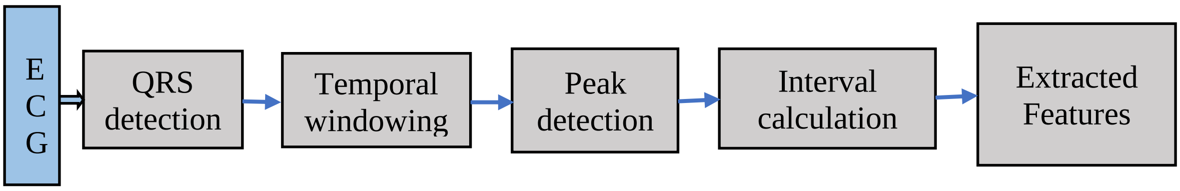


Figure 3.6 Feature Extraction model

The most prevalent ECG features that are utilized to detect changes in heart electrophysiological activities are listed in Table 3.5.

Table 3.4 ECG features with their description

Features	Description
Heart rate	Represents the number of heartbeats per second. The average heart rate of healthy person is 72 beats per minute [29].

Heart rate variability	Represents the response of the subject's heart to sympathetic and parasympathetic actions to maintain the heart rate.
P wave	The atria's depolarization is the source of P wave which has a duration of 0.07 to 0.18 seconds and amplitude range less than 0.20mV [28, 73]. The maximum point of P wave is P peak.
QRS complex	Depolarization of the ventricles is the source of QRS complex which has a duration of 0.06 to 0.12 seconds and amplitude range of 0.1 to1.5 mV [28, 73]. R peak is he maximum point of QRS complex.
T wave	The ventricle's repolarization is the source of T wave which has a duration of 0.1 to 0.25 seconds and amplitude less than 0.5mV [28, 73]. The maximum point of T wave is T peak.
PR interval	Has a duration of 0.12 to 0.20 seconds which starts at the beginning of the P wave and ends at the start of the QRS complex [28, 73].
QT interval	Has a duration of 0.32 to 0.36 seconds which runs from the beginning of QRS complex to the end of the T wave [73].
RR interval	Has a duration of 0.60 to 1 seconds which is the interval between the consecutive R peaks [90, 91].
PR segment	Has a duration of 0.02 to 0.10 seconds which runs from the end of the P wave to the start of the QRS complex [28, 73].
ST segment	Has a duration of less than 0.20 seconds which runs from the end of QRS to the beginning of the T wave [73].

3.5.1. QRS detection

Pan Tompkins algorithm is a time-domain algorithm that has an incredible advantage and is more genuine in detecting QRS peaks than other methods [89, 92, 93]. It consists of a series of lowpass filters, highpass filter, derivative filter, squaring, thresholding, and moving windowing procedures [33, 89, 92–94]. Figure 3.7 shows the Pan Tompkins model used in this study.

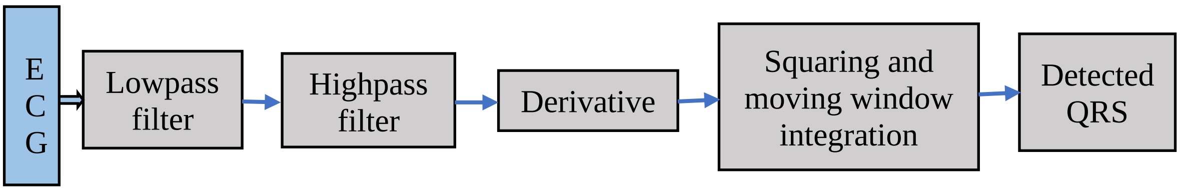


Figure 3.7 Pan Tompkins QRS complex detection model

Low pass filter: - The frequency range of the QRS complex is between 5Hz to 15Hz [33, 95]. High-frequency components greater than 15 Hz cannot be a part of the ECG signal QRS complex. The cut-off frequency of this filter is 15Hz. The low pass filter in pan Tompkins algorithm is represented by the transfer function in Equation 3.12.

$$H(z) = \frac{1}{32}\frac{(1-z^{-6})^2}{[1-z^{-1}]^2} \quad \text{Eq. 3.12}$$

The relation between the output of the filter with its input is represented by the formula in Equation 3.13.

$$y(n) = 2y(n-1) - y(n-2) + \frac{1}{32}[x(n) - 2x(n-6) + x(n-12)] \quad \text{Eq. 3.13}$$

High pass filter: - Low-frequency components less than 5Hz are not part of the QRS complex. The cut-off frequency of this filter is 5Hz. These low-frequency components of ECG signal such as P wave, T wave, and ST-segment were removed by applying pan Tompkins high pass filter [33, 95]. It is represented by the transfer function described in Equation 3.14.

$$H(z) = \frac{(1-z^{-32})}{[1-z^{-1}]} \quad \text{Eq. 3.14}$$

The input-output relation is represented by Equation 3.15.

$$y(n) = y(n-1) + x(n) - x(n-32) \quad \text{Eq. 3.15}$$

Derivative filter: - Because the derivative is the rate of change of amplitude with respect to time, it aids in enhancing the signal's high slope component (QRS) while suppressing the low slope components (P and T waves). This helps to prevent the detection of P and T peaks as R peaks [33]. The Pan Tompkins derivative operator is represented by Equation 3.16.

$$y(n) = \frac{1}{8}[2x(n) - x(n-1) - x(n-3) - 2x(n-4)] \quad \text{Eq. 3.16}$$

Squaring: - helps to suppress the small differences from T and P waves, to emphasize the large difference from the QRS complex, and make the result positive [33]. The output of squaring is given by Equation 3.17.

$$y(n) = [x(n)]^2 \quad \text{Eq. 3.17}$$

Moving window integration: - the preferred window duration for performing moving window integration is 150 mS [93, 96]. For sampling frequency of 1000Hz the number of samples in

150 mS is equal to 150 samples. The moving window integration was performed with a window length of 150 samples using the Equation described in Eq. 3.18.

$$y(n) = \frac{1}{n}\sum_{i=1}^{150} x(n-i) \quad \text{Eq. 3.18}$$

Adaptive thresholding: - adaptive thresholding best suits the pan Tompkins QRS detection algorithm [93]. The threshold value was calculated using adaptive thresholding method on the 150-sample window length. The data points less than the threshold value were assigned to “0” and the data points greater than the threshold value were assigned to “1”.

3.5.2. Feature detection and calculation

Calculating the temporal window: - the detected QRS peaks were counted iteratively. The heart rate is equal to the counted QRS peaks. The average beat duration in millisecond was calculated using Equation 3.19. The temporal window was calculated by subtracting some tolerance value from the average beat duration.

$$beat\ duration = 60\,\frac{sampling\ frequency}{heart\ rate} \quad \text{Eq. 3.19}$$

Peak detection (P, Q, R, S, T peaks): - MATLAB peak detector functions “max” and “min” were used for detecting the location and amplitude of maximum and minimum peaks within the calculated temporal moving windows. The maximum and the minimum amplitude points in each moving window were detected as R peaks and S peaks respectively.

Modified temporal windowing technique was used for detection of P, Q, and T peaks. Modified temporal windowing solved the problem of peak detection interference. For Q wave the modified temporal window was between the left margin of the calculated temporal window and the R peak location. For P wave the modified temporal window is between the left margin of the calculated temporal window and the Q peak location. Similarly, for T wave the modified temporal window is between S peak and right margin location of the calculated temporal window. Functions “max” and “min” were used to detect the location and amplitude of P, Q, and T peaks in their corresponding modified temporal windows. The inclination or declination points from the isoelectric line were detected as onset and offset point respectively. The intervals and segments were calculated from the onset and offset points of each waves. Finally, all the important calculated features were exported to an excel format from MATLAB workspace for further analysis.

3.6. Analysis

The heart rate, heart rate variability, R peak, QRS duration, P peak, T peak, PR interval, QT interval, RR interval, PR segment, and ST-segment were retrieved. These extracted features form 25 chewer subjects before and after chewing session, 25 control subjects before and after chewing session, 5 khat addicted subjects before and after rehabilitation therapy were sorted in their corresponding categories using Microsoft excel. Then each feature of chewers and controls before and after chewing session were arranged and plotted in the same figure. Similarly, each feature of khat addicted subjects before and after rehabilitation therapy were arranged and plotted in the same figure. The feature from different categories were plotted in the same plot to reveal the most significant changes. Qualitative observation of the effect of khat chewing and rehabilitation therapy from khat addiction on heart activity was made using the plots.

For ease of data manipulation, the ECG signal features of each category were averaged. The ECG features values of each control and chewer participants before and after the chewing session were compared. The difference in ECG features of the before chewing session and after chewing session was computed for both chewer and control subjects. To show the significance of the existed change the computed difference was expressed in percentage. The chewers average feature value changes between chewing session were compared to the controls average feature value changes. Similarly, for khat addicted subjects the average value of ECG signal features before and after rehabilitation therapy were compared. Again, the difference in signal features of khat addicted subjects before and after rehabilitation therapy was computed and expressed in percentage. The main deviations in the averaged feature values were observed. The feature value changes were interpreted and its indications were identified.

3.7. Materials

This study used a combination of hardware devices and software systems. The materials used along with their specifications are listed in Table 3.6. The computer served as the study's main working station, containing signal processing software such as MATLAB and BIOPAC.

Table 3.5 Materials needed for the study

No.	Materials	Specification
	Hardware	

1	Laptop computer	✓ RAM 8 GB, Hard disk 1 TB, With GPU, Speed 2.4 GHz, Having Keyboard backlight, Screen resolution 1024 X 768
2	BIO PACK	✓ MP36 module with its software
2	ECG machine with limb leads	✓ Standard ECG recording machine
3	External hard disc and flash	✓ 1 TB hard disk and 32 GB flash
Software		
1	MATLAB software	✓ MATLAB 2019a
3	Microsoft Excel	✓ Office 2019 premium

Chapter Four

4. Results and Discussion

4.1. Results

4.1.1. Pre-processing Results

4.1.1.1. Savitzky Golay smoothing

The Savitzky Golay smoothing filter was used to smooth the raw ECG data. The effect of Savitzky Golay filter is illustrated in Figures 4.1.

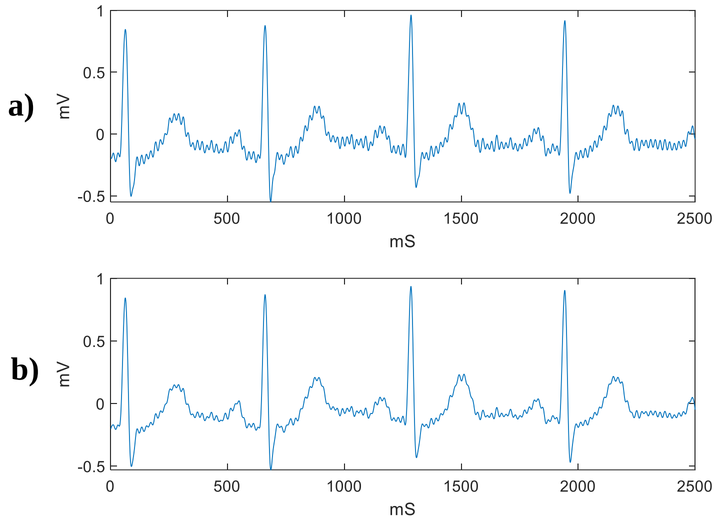


Figure 4.1 The raw (a), and Savitzky Golay smoothed (b) ECG signal

4.1.1.2. Discrete wavelet transforms denoising

After applying a discrete wavelet decomposition on the smoothed signal using Mayer mother wavelet the coefficients shown in Figure 4.2 were obtained.

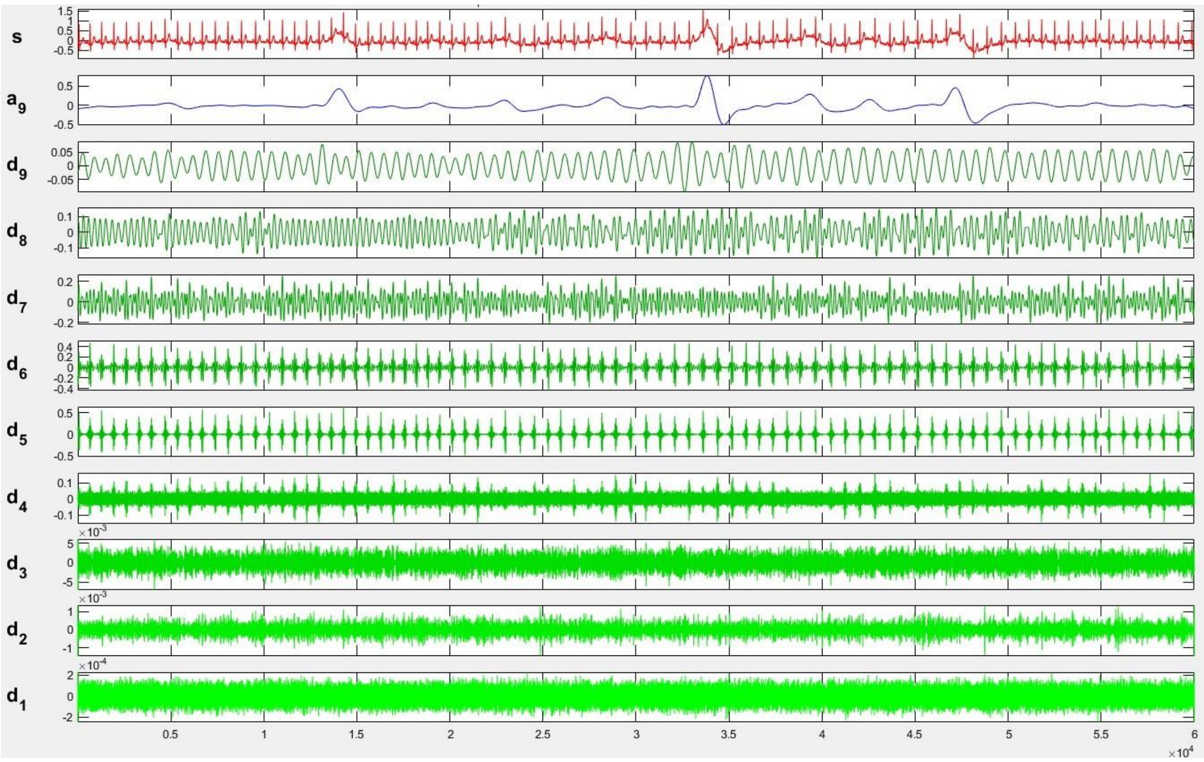


Figure 4.2 Wavelet coefficients before denoising

Using the selected thresholding method and technique (hard and heursure) the threshold values of each detail coefficient were calculated. For denoising each detail coefficient, the obtained threshold values were used. Table 4.1 presents the threshold values of each wavelet coefficient.

Table 4.1 Threshold value of detail coefficients

Detail coefficient	Threshold value
D9	0.000000250027911
D8	0.000000254316944
D7	0.000000051719642
D6	0.000000761261945
D5	0.000000729834243
D4	0.000000698187756
D3	0.000000667286123
D2	0.000000638742073
D1	0.000000614584796

Using the calculated threshold values each detail coefficient was denoised independently. Figure 4.3 shows the denoised coefficients.

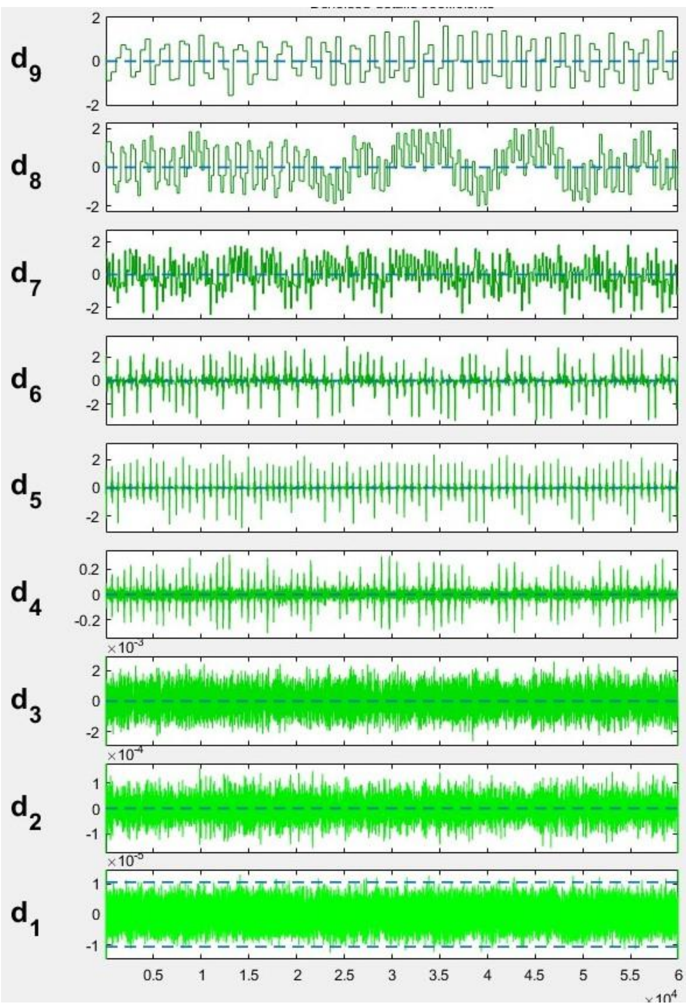


Figure 4.3 Denoised coefficients by their respective threshold value

Finally, the denoised signal was reconstructed from the denoised coefficients. Figure 4.4 shows the wavelet denoised signal.

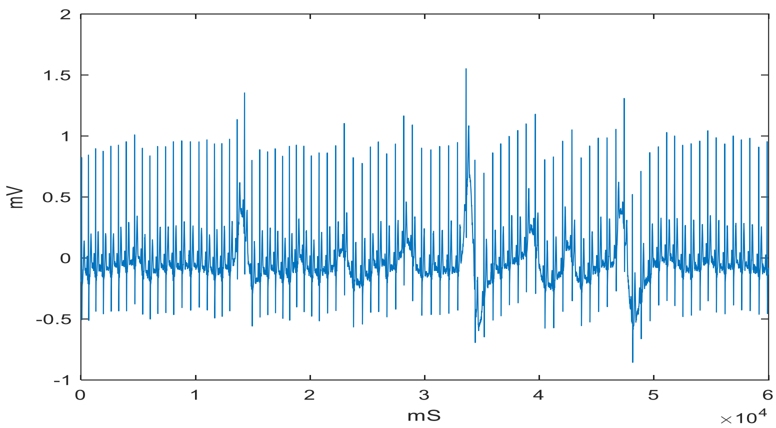
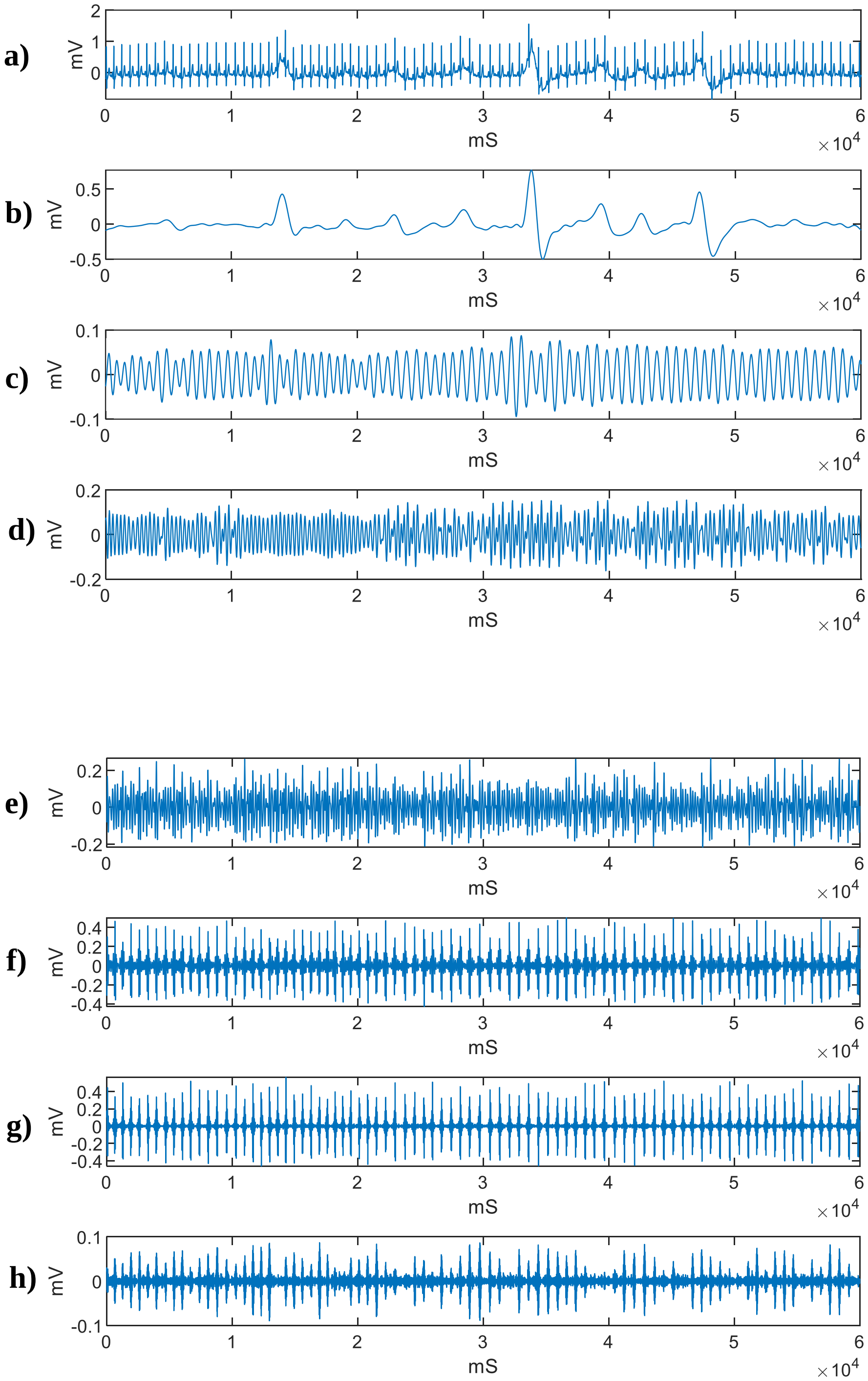


Figure 4.4 Reconstructed signal from denoised wavelet coefficients

4.1.1.3. Wavelet multiresolution analysis denoising

There was clearly visible residual contaminant noise within the wavelet denoised signal. The residual noises were removed using wavelet multiresolution analysis. Based on their frequency band, the wavelet multiresolution coefficients were decomposed as illustrated in Figure 4.5.



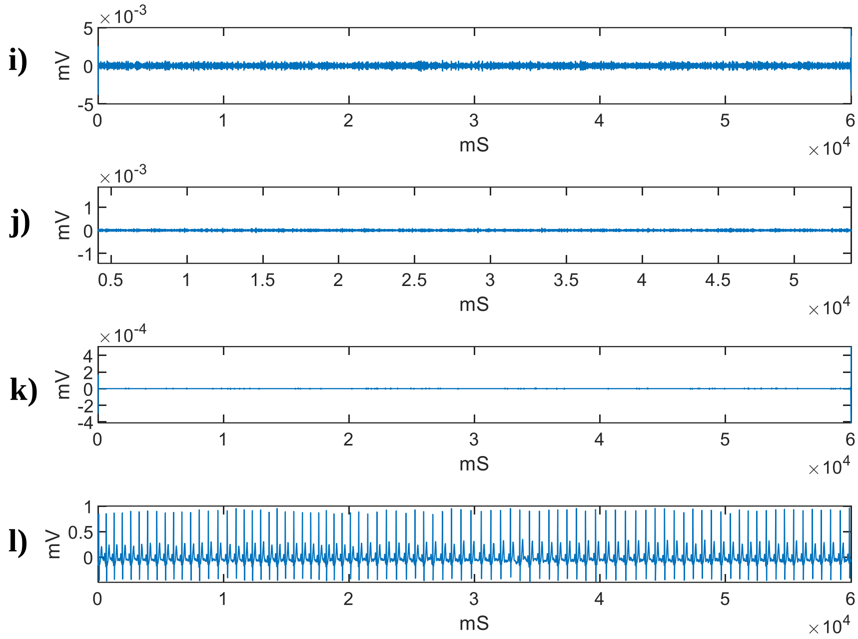


Figure 4.5 The input signal(a), approximate coefficient (b), detail coefficient d9 (c), detail coefficient d8 (d), detail coefficient d7 (e), detail coefficient d6 (f), detail coefficient d5 (g), detail coefficient d4 (h), detail coefficient d3 (i), detail coefficient d2 (j), detail coefficient d1 (k), and output signal (l) of wavelet multiresolution denoising.

The energy of each coefficient was then computed. Table 4.2, shows the energy contribution of each coefficients. The decomposition levels 1 to 4 were excluded for reconstruction since their energy contribution was minimal, accounting for less than 0.9 % of the total signal. The frequency range of approximate coefficient is below 1 Hz which was considered as a baseline wandering noise.

Table 4.2 Frequency range and relative energy of wavelet coefficients

Decomposed Coefficients	Frequency range in Hz	Relative energy contribution
Detail coefficient 1	250 – 500	0.00%
Detail coefficient 2	125 – 251	0.00%
Detail coefficient 3	62.4 – 125	0.00%
Detail coefficient 4	31.2 – 62.6	0.85%
Detail coefficient 5	15.6 – 31.3	16.81%
Detail coefficient 6	7.79 – 15.7	22.21%

Detail coefficient 7	3.9 – 7.83	14.04%
Detail coefficient 8	1.95 – 3.92	7.87%
Detail coefficient 9	0.975 – 1.96	3.02%
Approximation coefficient	0.0 – 0.976	35.20%

Finally, signal reconstruction was done by excluding the detail coefficients from 1 to 4 and the approximation coefficient. Figure 4.6 shows the reconstruction result of wavelet multiresolution denoising.

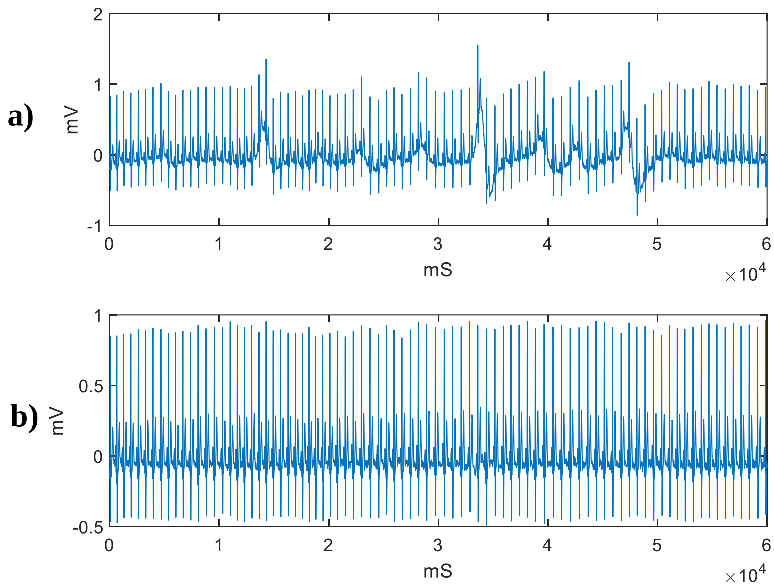
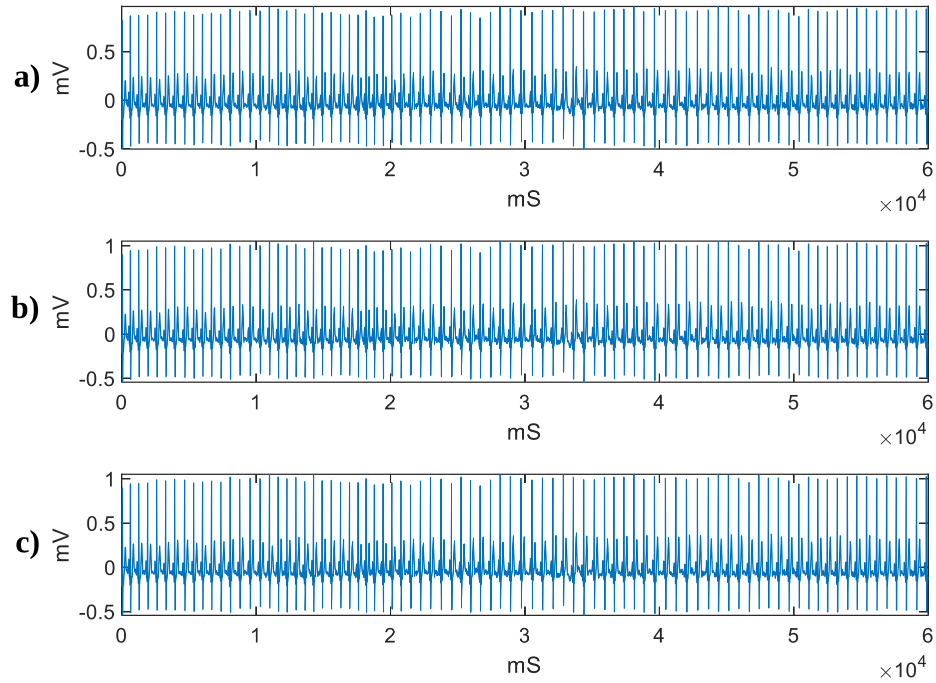


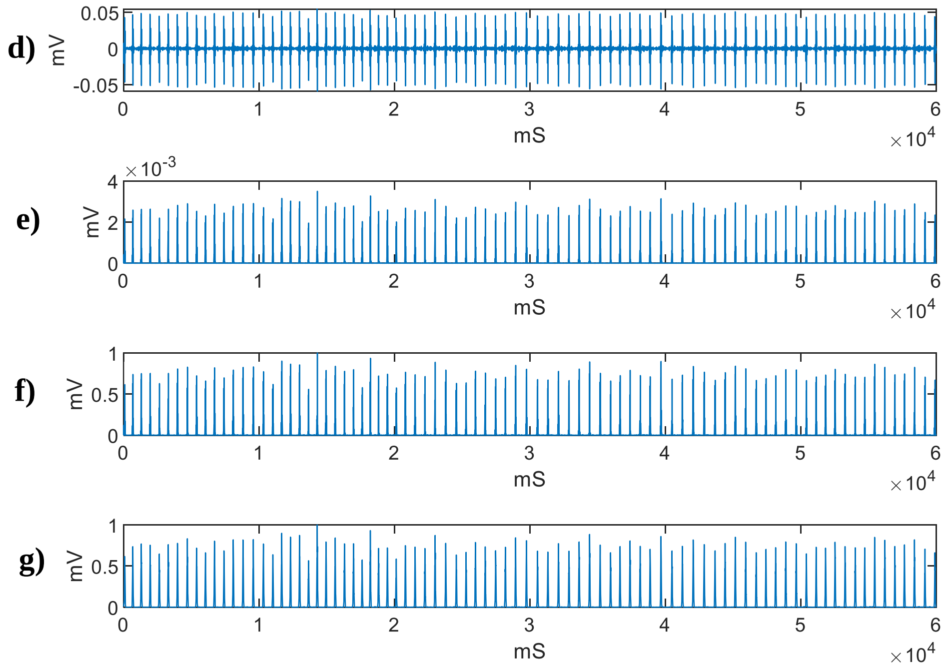
Figure 4.6 The input (a) and output (b) signals of wavelet multiresolution denoising

4.1.2. Feature extraction results

By suppressing other signal components, QRS peaks were successfully detected using pan Tompkins algorithm. The location and amplitude of other peaks were obtained using temporal peak detection methods. Then the location of the fiducial points (the starting and ending points of P, QRS, and T waves) were detected. Interval and segment durations were calculated using the location of the detected fiducial points. Figure 4.7 shows the outcomes of various steps of the feature extraction procedure.



a)
b)
c)
mV
mS
×10^4



d)
e)
f)
g)
mV
mS
×10^-3
×10^4

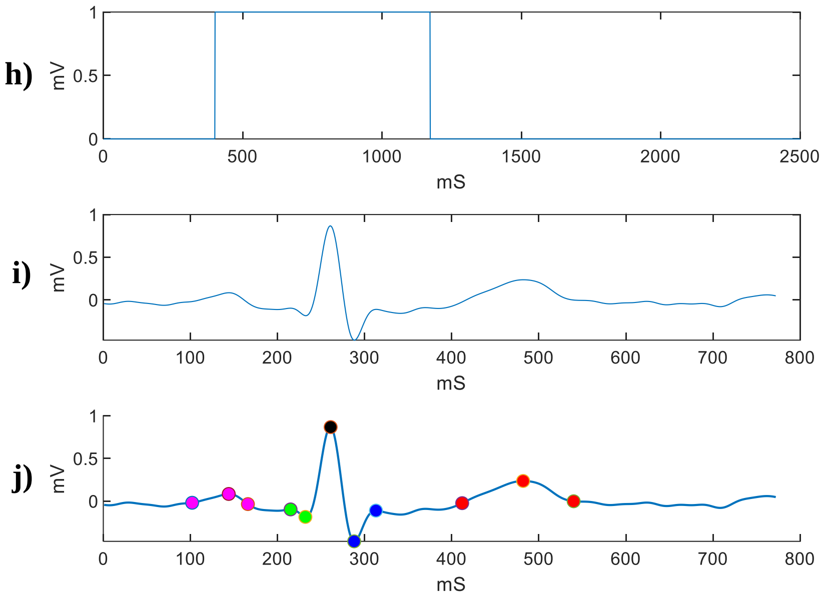


Figure 4.7 The input (a), lowpass filtered (b), highpass filtered (c) derivative filtered (d), squaring (e), normalization (f), moving average filter (g), moving window (h), the signal in window range (i), and the detected peaks and fiducial points (j) plots during the feature extraction procedure.

The detected peaks, calculated intervals and segments were exported as an excel format and that is the final output of feature extraction process. Table 4.3 shows extracted ECG features.

Table 4.3 Extracted ECG features

Data ID	B_01_1
Beat per minute (BPM)	70
Heart rate variability (HRV)	0.0098563
R peak	0.943810799
QRS duration	0.091971014
P peak	0.075933168
T peak	0.17084126
PR interval	0.145811594
QT interval	0.318246377
RR interval	0.844942029
PR segment	0.05415942
ST-segment	0.109

4.1.3. Result analysis

4.1.3.1. The effect of khat chewing on heart activity

The feature values were calculated from ECG signals of 25 chewer subjects before and after chewing, and 25 control (non-chewer) subjects before and after chewing sessions. Table 4.4 shows the extracted feature values for some of the collected ECG signals.

Table 4.4 ECG features of some chewer and control subjects before and after chewing session.

Features	KB01	KA01	CB01	CA01	KB11	KA11	CB11	CA11
BPM	70	83	76	77	68	81	74	73
HRV	0.0099	0.0071	0.0115	0.0095	0.0074	0.0049	0.0086	0.0045
R peak	0.9438	0.9020	0.9862	0.9964	0.9586	0.1816	0.7095	0.7168
QRS Complex	0.0920	0.0918	0.0917	0.0911	0.0933	0.0782	0.0889	0.0890
P peak	0.0759	0.0550	0.0837	0.0826	0.0764	0.0595	0.0597	0.0654
T peak	0.1708	0.2756	0.2262	0.2314	0.2262	0.1071	0.0455	0.0465
PR interval	0.1458	0.1192	0.1295	0.1299	0.1446	0.1310	0.1563	0.1529
QT interval	0.3182	0.3243	0.3217	0.3198	0.3314	0.3333	0.2924	0.2947
RR interval	0.8449	0.7132	0.7762	0.7687	0.8621	0.7283	0.8019	0.7979
PR segment	0.0542	0.0421	0.0595	0.0598	0.0589	0.048	0.0784	0.0750
ST segment	0.109	0.0992	0.1265	0.1251	0.1121	0.1277	0.1029	0.1051

The capital letters "**C**", and "**K**" were used to represent the control group and the khat chewer group respectively. The acronyms "**B**" and "**A**" represented the before and after chewing sessions respectively. The counting number were used to each subject based on recruitment order starting from **'01'**. For example, the annotation "**KB01**" represents the first recorded ECG signal from a khat chewer subject before chewing session. For handling the data more conveniently the feature values obtained were averaged and presented in Table 4.5.

Table 4.5 Average ECG features of chewer and control subjects before and after chewing session.

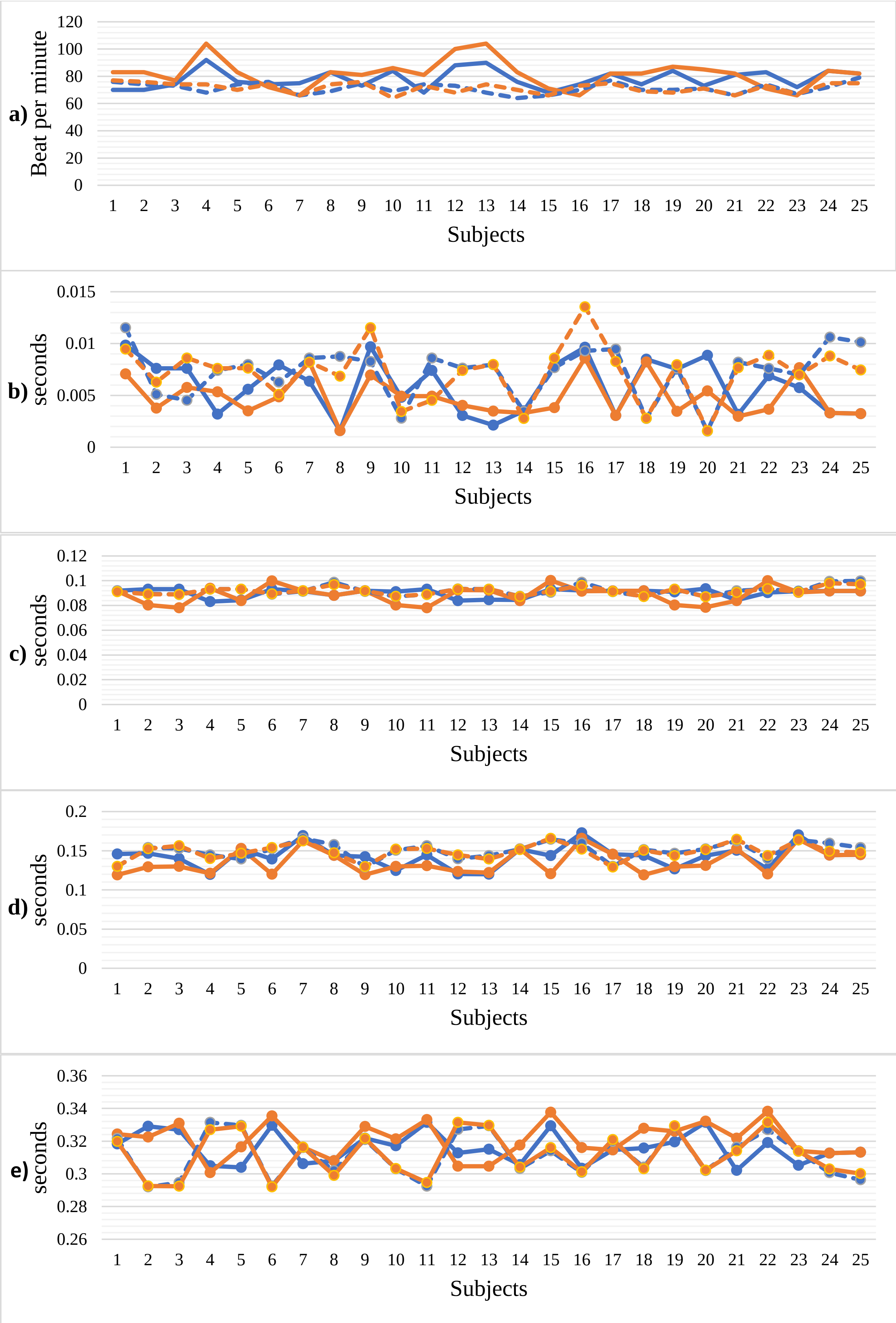
Feature	**KB**	**KA**	**KA-KB**	**% KA-KB**	**CB**	**CA**	**CA-CB**	**% CA-CB**
Heart Rate	78	81.76	3.76	4.82%	71.24	71.52	0.28	0.39%
HRV	0.0059	0.0049	0.0011	-18.24%	0.0072	0.0072	0.00004	-0.49%
R peak	0.8370	0.6690	0.1680	-20.07%	0.8149	0.8336	0.01863	2.29%
QRS duration	0.0901	0.0888	0.0013	-1.39%	0.0920	0.0917	0.00034	-0.37%
P peak	0.0841	0.0821	0.0020	-2.39%	0.0794	0.0797	0.00029	0.36%
T peak	0.1647	0.1650	0.0004	0.22%	0.1877	0.1959	0.00816	4.34%
PR interval	0.1430	0.1358	0.0072	-5.02%	0.1501	0.1488	0.00125	-0.83%

QT interval	0.3159	0.3208	0.0049	1.55%	0.3112	0.3115	0.00033	0.11%
RR interval	0.7605	0.7317	0.0288	-3.79%	0.8293	0.8258	0.00357	-0.43%
PR segment	0.0584	0.0514	0.0070	-11.96%	0.0664	0.0651	0.00125	-1.89%
ST segment	0.1088	0.1064	0.0023	-2.14%	0.1019	0.1025	0.00066	0.65%

The ECG signal features of chewer subjects before chewing session were averaged and denoted as **KB**. The abbreviation **KA** was used to denote the averaged ECG signal features of chewer subjects after chewing session. The averaged ECG features of control subjects before chewing and after chewing session were represented by **CB** and **CA** respectively. The notation **KA-KB** and **%KA-KB** were used to represent the ECG feature value difference in number and percentage between before and after chewing sessions respectively. Similarly, the **CA-CB** and **% CA-CB** were used to represent the number and percentage difference between before and after chewing session recorded ECG signal features.

The average value increments of chewers heart rate, T peak, and QT intervals after the chewing session are 3.76(4.82%), 0.0004(0.22%), and 0.0049(1.55 %) respectively. The average heart rate, R peak, P peak, T peak, QT interval, and ST segments increments for control subjects are 0.28 (0.39%), 0.0186 (2.29%), 0.00029 (0.36%), 0.00816 (4.34%), 0.00033 (0.11%), and 0.00066 (0.65%) respectively. After chewing khat the chewer's average heart rate variability, R peak amplitude, QRS duration, P peak amplitude, PR interval, RR interval, PR segment, and ST-segment values decreased by 0.0011 (18.24%), 0.1680 (20.07%), 0.0013 (1.39%), 0.0020 (2.39%), 0.0072 (5.02%), 0.0288 (3.79%), 0.0070 (11.96%), and 0.0023 (2.14%) respectively. After chewing session, the average heart rate variability, QRS duration, PR interval, RR interval, and PR segment of the control subjects decreased by 0.00004 (0.49%), 0.00034 (0.37%), 0.00125 (0.83%), 0.00357 (0.43%), and 0.00125 (1.89%) respectively.

Plotting the acquired feature values of different (chewer and control before and after chewing session) categories revealed the most significant changes. The results illustrate that after chewing session the chewer participants' R peak, HRV, and PR segment were considerably lower than the control subjects. Figures 4.8 and 4.9 show the changes in each ECG signal features of chewer and control subjects before and after the chewing session.


a)
Beat per minute
120
100
80
60
40
20
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Subjects
b)
seconds
0.015
0.01
0.005
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Subjects
c)
seconds
0.12
0.1
0.08
0.06
0.04
0.02
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Subjects
d)
seconds
0.2
0.15
0.1
0.05
0
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Subjects
e)
seconds
0.36
0.34
0.32
0.3
0.28
0.26
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Subjects

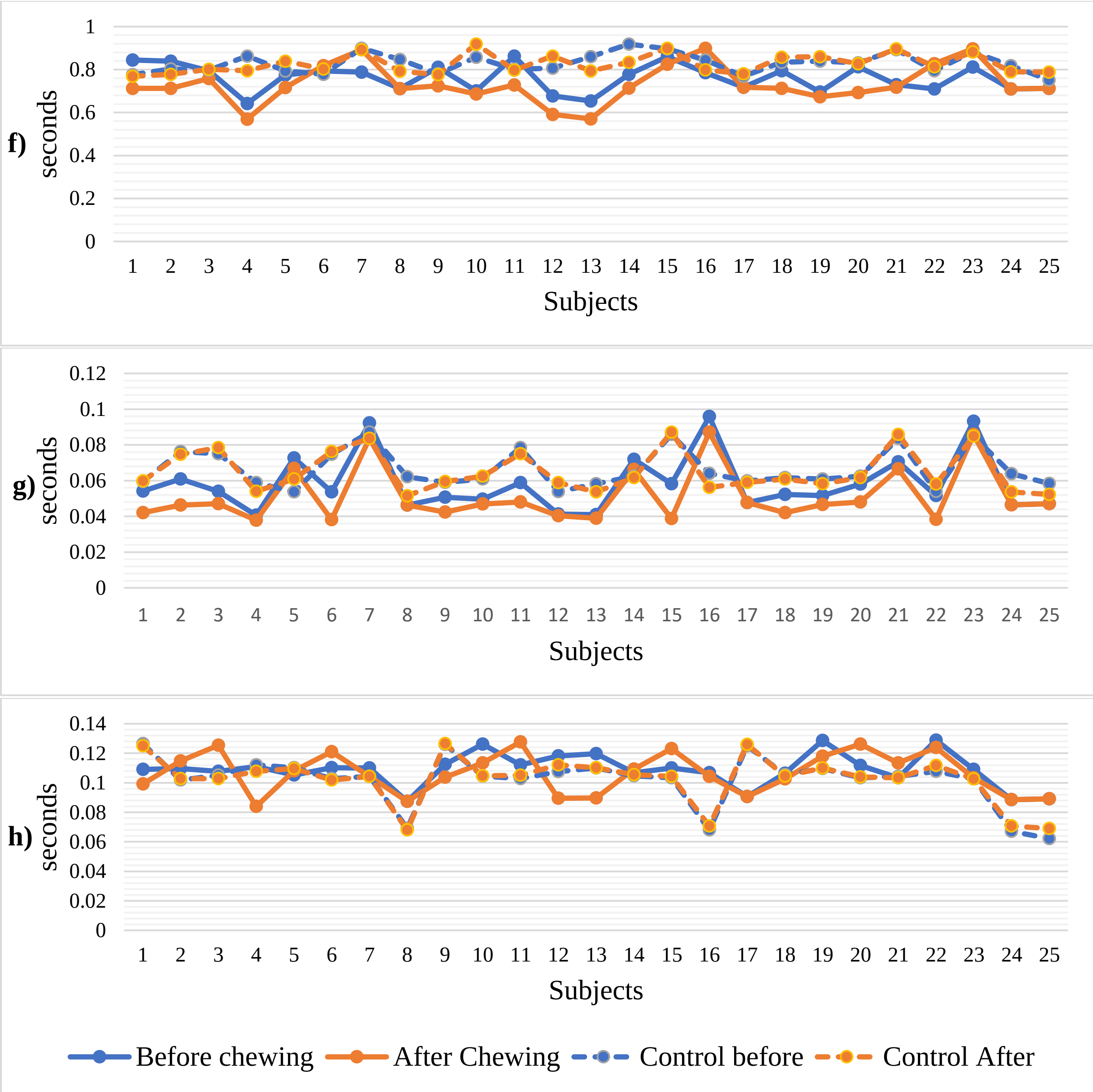


Figure 4.8 The heart rate (a), heart rate variability (b), QRS complex duration (c), PR interval (d), QT interval (e), RR interval (f), PR segment (g), and ST segment values of khat chewer and control (non-chewer) subjects before and after khat chewing sessions.

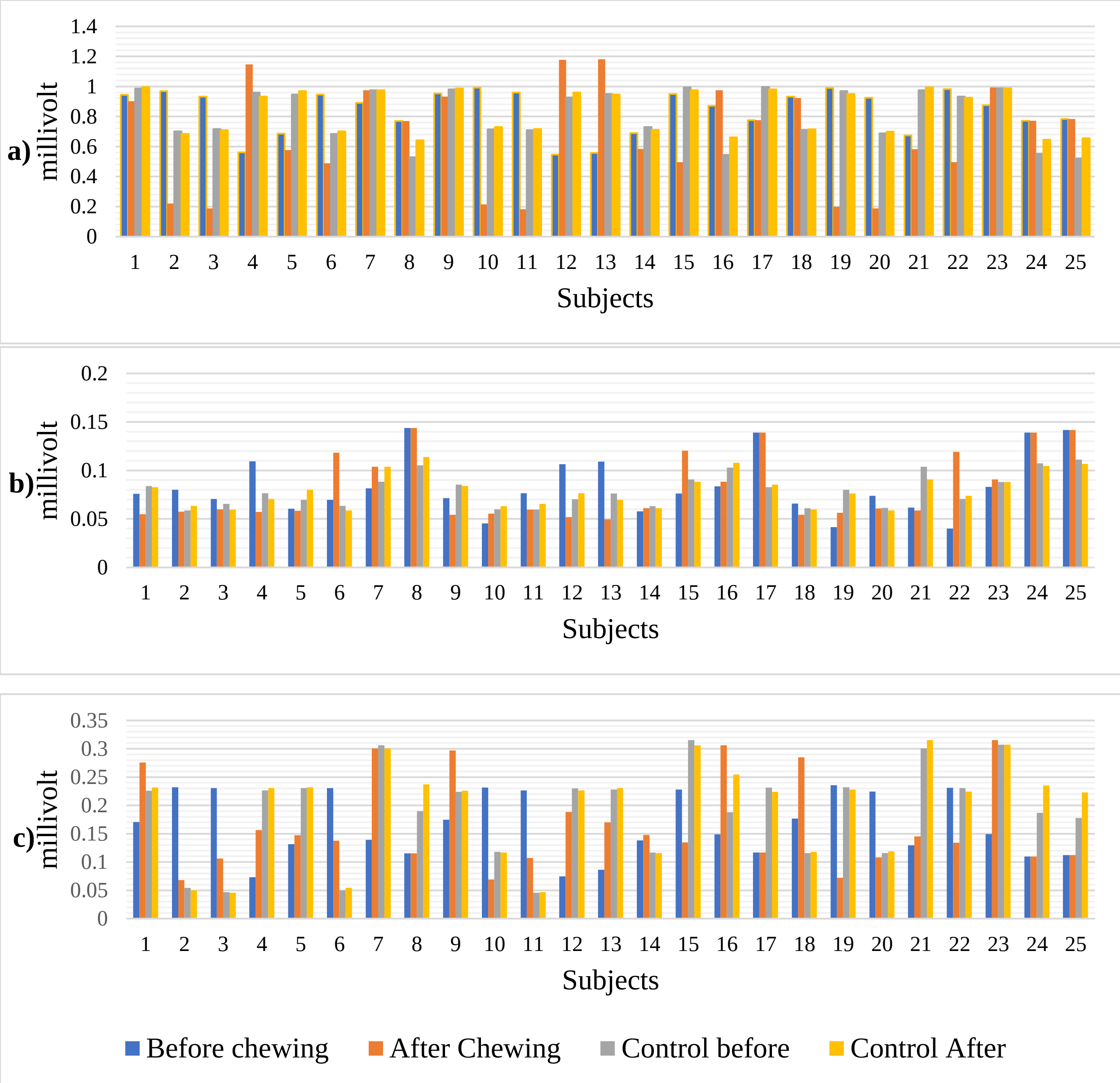


Figure 4.9 The R peak amplitudes (a), P peak amplitudes (b), and T peak amplitudes (c) of khat chewer and control subjects before and after khat chewing sessions.

4.1.3.2. The effect of rehabilitation therapy on khat addicted subjects' heart activity

Features were extracted from the ECG signals of 5 khat-addicted patients before they started rehabilitation therapy (at the time of admission) and after one week of rehabilitation therapy. Some of the extracted ECG features from khat addicted subjects are shown in Table 4.6.

Table 4.6 ECG features from some khat addicted subjects

Features	RB_01	RA_01	RB_03	RA_03
BPM	99	84	79	72
HRV	0.0050	0.0072	0.0088	0.0119
R peak	1.1782	0.9986	0.9241	0.9542
QRS Complex	0.0924	0.0909	0.0921	0.0919
P peak	0.0490	0.0438	0.0541	0.0716
T peak	0.1807	0.2415	0.2954	0.1747
PR interval	0.1228	0.1252	0.1200	0.1423
QT interval	0.3047	0.3187	0.3291	0.3216
RR interval	0.5968	0.6987	0.7430	0.8104
PR segment	0.0397	0.0501	0.0430	0.0506
ST segment	0.0896	0.1280	0.1037	0.1124

The letters "**R**", “**B**” and “**A**” represent khat addicted subject, before chewing session and after chewing sessions respectively. The counting numbers were used to each subject based on recruitment order starting from ‘01’. For example, the annotation "**RB01**" represents the first recorded ECG signal from a khat addicted subject before rehabilitation therapy. To make data management easier, the feature values from khat addicted subjects before and after rehabilitation therapy were averaged and presented in Table 4.7.

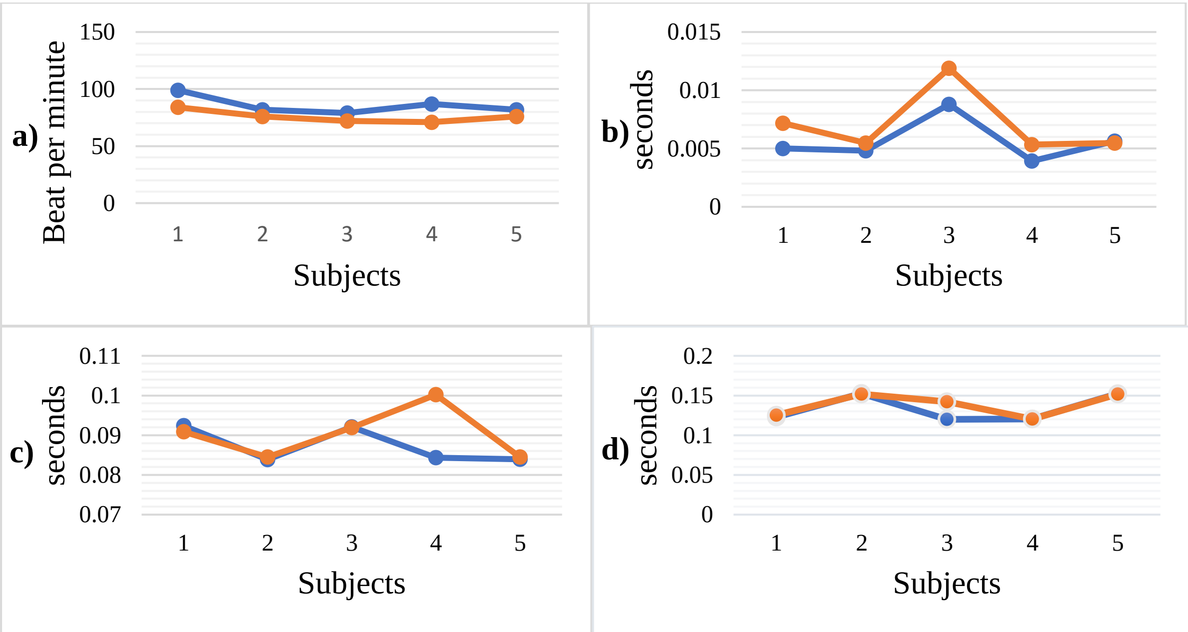
Table 4.7 The average values of ECG features before and after rehabilitation therapy

Feature	**RB**	**RA**	**RA-RB**	**%RA-RB**
Heart rate	85.8	75.8	10	-11.66%
HRV	0.0056	0.0071	0.0014	25.43%
R peak	0.7654	0.7687	0.0033	0.43%
QRS duration	0.0873	0.0904	0.0030	3.49%
P peak	0.0646	0.0704	0.0058	8.94%
T peak	0.1710	0.1664	0.0047	-2.72%
PR interval	0.1336	0.1383	0.0047	3.49%
QT interval	0.3173	0.3180	0.0007	0.22%
RR interval	0.6908	0.7774	0.0866	12.53%
PR segment	0.0514	0.0566	0.0052	10.09%
ST segment	0.1068	0.1155	0.0087	8.13%

The abbreviations **"RB"**, **"RA"**, **"RA-RB"** and **"%RA-RB"** were used to represent the averaged ECG signal features of before rehabilitation therapy, after rehabilitation therapy, the difference between after and before rehabilitation therapy, the percentage difference between after and before rehabilitation therapy sessions respectively.

The results shows that rehabilitation therapy reduced heart rate by an average value of 10 BPM (11.66%) from an average of 85.8 BPM, and T peak value by 0.0047mV (2.72%) from an average amplitude of 0.171017 mV. One of the participants was tachycardic before rehabilitation therapy and becoming normal after therapy.

After rehabilitation therapy increments of 0.0014S (25.43%), 0.0033mV (0.43%), 0.0030S (3.49%), 0.0058mV (8.94%), 0.0047S (3.49%), 0.0007S (0.22%) and 0.0866 (12.53%) have been observed for heart rate variability, R peak, QRS duration, P peak, PR interval, QT interval, RR interval respectively. Figures 4.10 and 4.11 show the ECG feature changes following rehabilitation therapy.



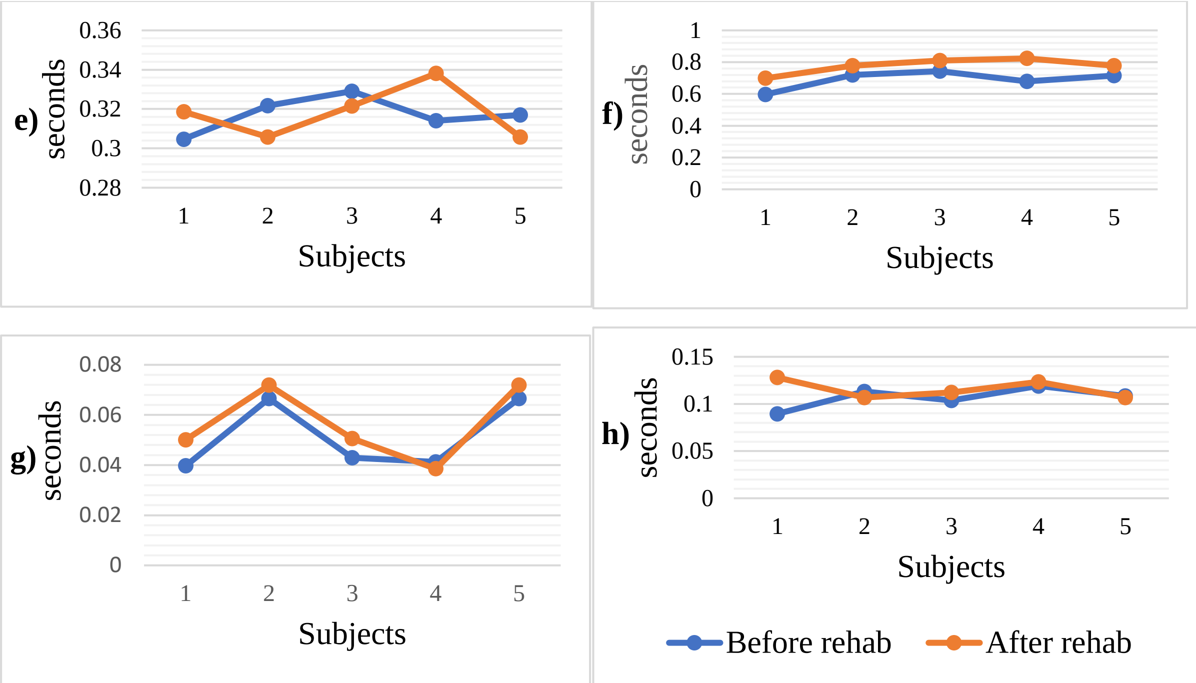


Figure 4.10 The heart rate (a), heart rate variability (b), QRS complex duration (c), PR interval (d), QT interval (e), RR interval (f), PR segment (g), and ST segment values of khat addicted subjects before and after rehabilitation therapy.

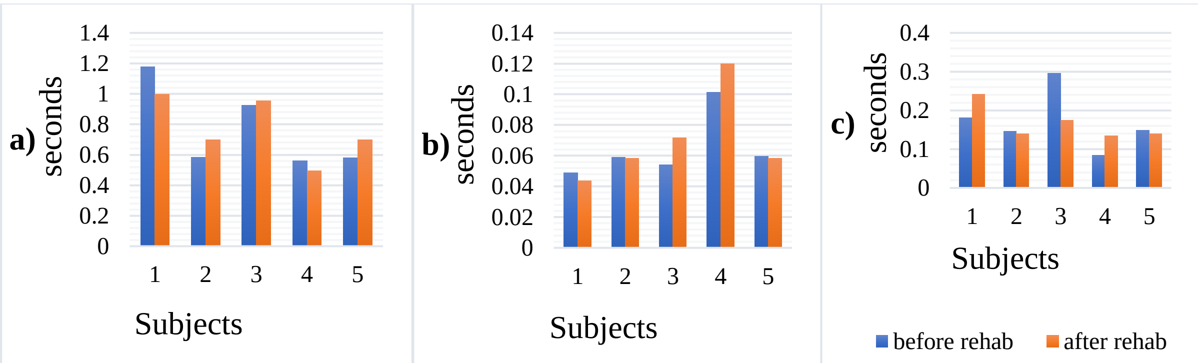


Figure 4.11 The R peak amplitudes (a), P peak amplitudes (b), and T peak amplitudes (c) of khat addicted subjects before and after rehabilitation therapy.

4.2. Discussion

The objective of this study was to investigate the effect of khat and rehabilitation therapy from khat addiction on heart activity. This study was conducted by recording ECG signals from the selected subjects. The recorded signals were denoised to remove the disturbances and noises. ECG features were extracted form the denoised signal. Analysis was done using the extracted ECG features.

The analysis findings indicate that after the chewing session, the chewers' heart rate increased by an average of 3.76 BPM (4.82 %) compared to the average heart rate value of the before chewing session. All the chewer subjects were normal before they chewed, however 3 (12%) of them developed tachycardia following the chewing session. Between before and after chewing sessions, the average heart rate of the control volunteers was changed only by 0.28 BPM (0.39%). This reveals that khat has tachycardia (arrythmia) inducing impact. The study conducted previously on 60 people using "Beleche," also showed khat chewing reduces the RR interval by 9% and increases the ventricular depolarization velocity by 11%, which raises heart rate [10]. Moreover, a study done previously on 30 cardiac patients shows non sustained ventricular tachycardia (arrythmia or abnormal rhythm) occurred on 23.3% of the subjects on khat chewing day and 6.6% on khat-free days [15, 56].

For those who were chewing the average heart rate variability before chewing session was 5.9 mS and after the chewing session it was 4.9 mS. The heart rate variability of khat chewers dropped by 1 mS (18.24%) after chewing session. Whereas the average heart rate variability of control participants, is increased by 0.04ms (0.49%) between before and after chewing sessions. This finding indicates that consuming khat reduces heart rate variability. The cardiac stress caused by khat chewing has lowered the subject's sympathetic and parasympathetic efforts to maintain heart rate variability [97, 98]. Lowered sympathetic and parasympathetic response could initiate cardiac failure[99, 100].

The average R peak value of the chewer subjects was reduced by a value of 0.168 mV (20.07%) after the chewing session when compared to before the chewing session. The average R peak value of the control subjects was increased by 0.0186 mV (2.29%) after chewing session compared to the before chewing session. This indicates that chewing khat has a significant impact of reducing R peak amplitude to cause premature ventricular contraction, arrythmia, and heart failure. The R peak is expected to have a normal amplitude of roughly 1mV [73, 101, 102]. Chewers have a lower R peak amplitude than non-chewers, indicating that they are more susceptible to premature ventricular contraction or bundle branch block ventricular ectopic [101].

Chewer subjects had an average QRS duration of 90.1ms before the chewing session and 88.8ms after the chewing session. Between before and after chewing sessions, the QRS duration decreased by 1.3mS (1.39 %). The average QRS duration of the control subjects, on the other hand, increased by 0.34mS (0.37%) between before and after chewing sessions. This reveals that consuming khat reduces the QRS duration, which could lead to premature ventricular contraction and heart failure. Studies had also proved that khat chewing has a substantial effect on lowering QRS duration and causing premature ventricular contraction [101, 103].

Chewers' P peak decreased by an average of 0.002 mV (2.39%) after chewing session compared to before chewing session, while control participants' P peak increased by 0.00029 mV (0.36 %) after chewing session. Chewers' average T peak increases by 0.0004 mV (0.22 %) after a chewing session compared to before the chewing session. T peak was reduced by 0.00816 mV (4.34 %) after chewing session for controls. This reveals that consuming khat reduces P peak amplitude whereas the T peak shows an insignificant increment. The amplitudes of the P and T peaks are in the usual range [73, 101]. As a result of this discovery, khat chewing has no substantial influence on atrial depolarization or ventricular repolarization.

Before and after chewing sessions, the chewers' average PR intervals were 143mS and 135.8mS, respectively. This demonstrates that khat chewing caused a PR interval reduction of 7.2mS (5.02 %). The PR interval following a chewing session increased by 1.25 mS (0.83 %) for control participants. The normal PR interval is between 0.12 and 0.2 seconds [73, 101, 102]. Chewers' average QT interval increased by 4.9mS (1.55 %) after a chewing session compared to before chewing session. For the control subjects there was a 0.33mS (0.11 %) QT interval increment between before and after chewing sessions. The results showed that consuming khat seemed to have no effect on the QT interval. The usual QT interval lasts between 300 and 440 mS [73, 101, 102]. As indicated in Table 4.5, the QT intervals found in this investigation are within the normal range.

Before and after chewing sessions, the average value of chewers PR segment was 58.4mS and 51.39mS, respectively. The PR interval value was decreased by 7mS (11.96 %) after chewing session. The average PR segment value of control subjects decreased by 1.25mS (1.89%) after chewing session compared to before chewing session value. This suggests that khat chewing causes a significant PR segment reduction. The PR segment's usual range is predicted to be between 20 and 100 mS [73]. Chewers' ST-segment was reduced by 2.3mS (2.14 %) after chewing khat compared to before chewing. For the control subjects an average increment of 0.66mS (0.65 %) was observed on the ST-segment after chewing session while comparing it to the before chewing session. The results showed that Chewing khat reduces ST segment insignificantly. Usually ST segment lasts between 50 and 150 mS [73, 102]. In this study the chewers' average ST-segment after chewing is in the normal range, as shown in Table 4.5.

The heart rate and T peak value both decreased after rehabilitation therapy compared to before rehabilitation therapy, indicating that heart activity has improved. One of the five participants was tachycardic (99 beats per minute) prior to rehabilitation, but after rehabilitation therapy, his heart rate decreased and returned to normal (84 beats per minute) range. The ECG features of the addicted patient, such as heart rate variability, R peak amplitude, QRS duration, P peak amplitude, PR interval, RR interval, PR segment, and ST-segment, showed a considerable increase to indicate the restoration addict’s heart activity to the normal condition following rehabilitation therapy. Studies also proved the improvements of heart activity and cardiovascular system after a successful rehabilitation therapy [36, 37].

Chapter Five

5. Conclusion and Recommendation

5.1. Conclusion

Digital signal processing techniques were used to investigate the effect of khat and khat addiction rehabilitation therapy on cardiac activity. Chewers and control subjects' signals were recorded before and after the chewing session. The ECG signal was smoothed using the Savitzky Golay filter. The output signal of Savitzky Golay filter was denoised using the discrete wavelet transforms filtering method with decomposition level nine, hard thresholding method, and heursure thresholding technique. The wavelet multiresolution analysis denoising method was used to filter the residual noise following wavelet denoising. Then, using a time domain ECG feature extraction method, ECG features were extracted. The values of the acquired features were used to detect changes in ECG signal. After chewing khat, the average heart rate of the chewers was increased by 4.82%, with 3 subjects out of 25 were prone to tachycardia. 1.39% QRS duration and 20.07% R-peak amplitude reduction were observed after chewing session. Moreover, heart rate variability was reduced by 18.24% indicating the effect of khat on suppressing sympathetic and parasympathetic nerve actions. After rehabilitation therapy, the average heart rate was reduced by 11.66%, while heart rate variability, QRS duration, and RR interval were increased by 25.43%, 3.49%, and 12.53%, respectively. The findings of this study show that chewing khat solely could cause premature ventricular contraction, arrythmia, and cardiac failure. Additionally, rehabilitation therapy could restore khat addicted subject’s heart activity to the normal range.

5.2. Recommendation

This study investigated the effect of khat solely on the heart activity. Moreover, the effect of rehabilitation therapy on khat addict’s heart activity was investigated. By using this study as springboard, it is recommended to collect community representative samples for investigating the effect of khat and rehabilitation therapy on the heart activity. The results of this study strongly advise khat chewers to stop chewing before developing a heart problem. Furthermore, this report advises khat addicts should immediately quit chewing and seek treatment.

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Appendices A

Subject information sheet for khat chewing part

Name __________________________________ Age ________ sex _______ chewing history ______________________________ alcohol consumption history ______________________________ coffee consumption history _______________________ drug usage _____________________ annotated ECG signal names ______________ before chewing and _______________ after chewing

Subject information sheet for khat rehabilitation therapy part

Name __________________________________ Age ________ sex _______ chewing history ______________________________ alcohol consumption history ______________________________ coffee consumption history _______________________ drug usage _____________________ annotated ECG signal names

1. At the time rehabilitation therapy started _______________
2. After 8 days _________________

Informed consent from the subject for the khat chewing part

Mr. Ewunate has got my full permission to record the ECG signal from me before I started chewing khat and after I get excited. I am willing for my ECG signal to be used by Mr. Ewunate's research.

Name ___________________________

Signature _____________________

Date _____________________

የግለሰቡ/ቧ የፈቃደኝነት ቃል ለ ጫት ተጸእኖ ጥናት

አቶ እውነቴ ጫት ከመቃሜ በፊት እና ከመረቀንኩ በኋላ የኢሲጅ ሲናል ከእኔ እንዲቀዳ እና ለ ምርምሩ እንዲጠቀመው ሙሉ ፈቃዴን ሰጥቸዋልሁ።

ስም______________________________

ፊርማ __________________________

ቀን ___________________________

Informed consent from the subject for rehabilitation therapy part

Mr. Ewunate has got my full permission to record ECG signals from me now and after a week. I am willing for my ECG signal to be used by Mr. Ewunate's research.

Name ___________________________

Signature ____________________

Date ____________________

የግለሰቡ/ቧ የፈቃደኝነት ቃል ለ ማገገሚያ ህክምና ጥናት

አቶ እውነቴ ከ ዛሬ እና የዛሬ ሳምንት የኢሲጅ ሲናል ከእኔ እንዲቀዳ እና ለ ምርምሩ እንዲጠቀመው ሙሉ ፈቃዴን ሰጥቸዋልሁ።

ስም______________________________

ፊርማ __________________________

ቀን ___________________________

Appendices B

The subject eligibility checklist

For the effect of chewing khat on the heart activity part of the research

Criteria	**Yes**	**No**
Fully voluntary		
Didn't have any confirmed case of CVDS		
Free from any addiction and drug consumption		
Age range between 18 and 35 years old		
Didn't take khat at least for the past 7 days		
Didn't take alcohol at least for the past three days		
Didn't take alcohol at least for the past three days		
Didn't take coffee at least for the past 36 hours		
The chewing frequency should be once a week or less		

For the effect of rehabilitation therapy on the heart activity part of the research

Criteria	Yes	No
Fully voluntary		
In addiction state		
Starting rehabilitation therapy		
Addicted to khat only		

Appendices C

Signed Approvals

Declaration

I declared this research proposal with the title of "**Analysing the Effects of Khat and Rehabilitation Therapy for Khat Addiction on Heart Activity**" as my original work and I assure it with my signature.

Ewunate Assaye Kassaw

Signature------------------------------ Date---09-04-2021

On behalf of the School of Biomedical Engineering at Jimma University, Jimma Institute of Technology we the advisors of this research proposal entitled "**Analysing the Effects of Khat and Rehabilitation Therapy for Khat Addiction on Heart Activity**" and I, the evaluator, confirm that this research proposal is approved as MSc. thesis for the student.

Advisor: Gizeaddis Lamesgin (Ph.D.) Signature---------------------------- Date-12/04/2021

Co-Advisor: Genet Tadesse (MSc.) Signature---------------------------- Date------------------

Jimma University Institute of Health

Institutional Review Board

Ref.No: JHRPGD/75/21

Date: 20/4/2021

To: **Ewunate Assaye**

Subject: Ethical Approval of Research Protocol

The IRB of Institute of Health has reviewed your research project **"Analyzing the Effects of Khat and Rehabilitation Therapy for Khat Addiction on Heart Activity"**

Thus, this is to notify that this research protocol as presented to the IRB meets the ethical and scientific standards outlined in national and international guidelines. Hence, we are pleased to inform you that your research protocol is ethically cleared.

We strongly recommend that any significant deviation from the methodological details indicated in the approved protocol must be communicated to the IRB before it has been implemented.

With Regards!

Million Tesfaye (MSc, PHD)
IRB chairperson
Tel: +251 913542906
E-mail: mtesfaye1@gmail.com

Tel. +251-47 11 114 57 PBX. +251471111456-60- Fax: +2514711114 50 +251471112040 P.O.Box 378 JIMMA, ETHIOPIA e-mail: ero@ju.edu.et website: http://www.ju.edu.et

Ref. No. PM23/385

Date: 24/01/2014

Institutional Review Board (IRB) of St. Paul's Hospital Millennium Medical College (SPHHMC)

Ethical Clearance

Research Title: Analyzing the effects of khat and rehabilitation therapy for khat addiction on heart activity

Principal Investigator: Ewunate Assaye

The IRB of SPHMMC has reviewed the above mentioned research proposal and made the following decision:

- Approved:- ________x___________
- Approved with recommendation:- ___________
- Approved on condition :-____________________
- Disapproved:- ____________________________

The decision is valid for 12 months and the research should be conducted in compliance with the protocol/proposal approved by the IRB of SPHMMC. Any subsequent revision/amendment of the protocol/proposal needs approval before conduct of the research. The researcher should also submit written summaries of the research status to the IRB every 03 months. Upon the conclusion of the study, manuscripts and thesis work to the final/completed research project needs to be submitted to the IRB.

IRB Chair:

Signature: ______________________

Date: September/22, 2021

Cc:

- Vice Provost for Academic and Research
- IRB
- Ewunate Assaye

SPHMMC

Appendices D

Subject Information Sheet

Title: - Analysing the effect of khat and rehabilitation therapy from khat addiction on heart activity

Recruited subject's information for the khat chewing part of the study

No.	Subject ID	Sex	Age	BMI	Occupation	ECG	Medicine
1	KB01	Male	29	18.60	Student	Normal	No
2	CB01	Male	29	19.00	Student	Normal	No
3	KB02	Male	26	21.70	Civil servant	Normal	No
4	CB02	Male	26	21.60	Civil servant	Normal	No
5	KB03	Male	29	23.86	Civil servant	Normal	No
6	CB03	Male	29	24.00	Civil servant	Normal	No
7	KB04	Female	27	19.90	Student	Normal	No
8	CB04	Female	27	19.60	Student	Normal	No
9	KB05	Female	25	23.60	Student	Normal	No
10	CB05	Female	25	23.60	Student	Normal	No
11	KB06	Male	29	23.60	Civil servant	Normal	No
12	CB06	Male	29	23.90	Civil servant	Normal	No
13	KB07	Male	24	20.60	Student	Normal	No
14	CB07	Male	24	20.61	Student	Normal	No
15	KB08	Male	26	19.20	Student	Normal	No
16	CB08	Male	26	19.30	Student	Normal	No
17	KB09	Male	26	21.60	Student	Normal	No
18	CB09	Male	26	21.30	Student	Normal	No
19	KB10	Male	29	23.03	Student	Normal	No
20	CB10	Male	29	22.80	Student	Normal	No
21	KB11	Male	30	22.87	Civil servant	Normal	No
22	CB11	Male	30	22.60	Civil servant	Normal	No
23	KB12	Female	28	22.00	Student	Normal	No
24	CB12	Female	28	21.90	Student	Normal	No
25	KB13	Female	26	21.60	Student	Normal	No

26	CB13	Female	26	21.60	Student	Normal	No
27	KB14	Male	27	22.73	Civil servant	Normal	No
28	CB14	Male	27	22.81	Civil servant	Normal	No
29	KB15	Male	29	22.60	Student	Normal	No
30	CB15	Male	29	22.70	Student	Normal	No
31	KB16	Male	27	21.00	Student	Normal	No
32	CB16	Male	27	21.20	Student	Normal	No
33	KB17	Male	28	19.60	Student	Normal	No
34	CB17	Male	28	19.60	Student	Normal	No
35	KB18	Male	22	19.30	Student	Normal	No
36	CB18	Male	22	19.35	Student	Normal	No
37	KB19	Male	28	20.36	Civil servant	Normal	No
38	CB19	Male	28	20.60	Civil servant	Normal	No
39	KB20	Female	26	18.60	Student	Normal	No
40	CB20	Female	26	18.80	Student	Normal	No
41	KB21	Female	23	21.10	Student	Normal	No
42	CB21	Female	23	21.10	Student	Normal	No
43	KB22	Male	23	19.60	Student	Normal	No
44	CB22	Male	23	19.60	Student	Normal	No
45	KB23	Male	23	19.81	Student	Normal	No
46	CB23	Male	23	19.60	Student	Normal	No
47	KB24	Male	25	19.00	Student	Normal	No
48	CB24	Male	25	19.10	Student	Normal	No
49	KB25	Male	27	23.00	Student	Normal	No
50	CB25	Male	27	23.00	Student	Normal	No

Recruited subject information for the rehabilitation therapy case study part

No.	Subject ID	Sex	Age	BMI	Occupation	ECG	Medicine
1.	RB01	Male	38	17.9	Private	Tachycardia	No
2.	RB02	Male	31	19	Health worker	Normal	No
3.	RB03	Male	28	19.2	Private	Normal	No
4.	RB04	Female	35	24	Private	Normal	No
5.	RB05	Male	23	19	Private	Normal	No
6.	RA01	Male	38	18.5	Private	Normal	Yes
7.	RA02	Male	31	19.3	Health worker	Normal	Yes
8.	RA03	Male	28	19.2	Private	Normal	Yes
9.	RA04	Female	35	23.4	Private	Normal	Yes
10.	RA05	Male	23	19	Private	Normal	Yes