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FATIH UNIVERSITY
INSTITUTE OF BIOMEDICAL ENGINEERING

EVALUATING EFFECT OF WII EXERCISE ON PARKINSON'S DISEASE-RELATED TREMOR SIGNALS

ESRA ÖZBEK

MSc THESIS
BIOMEDICAL ENGINEERING PROGRAMME

İSTANBUL, SEPTEMBER / 2014

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THESIS ADVISOR
ASSIST. PROF. DR. ŞÜKRÜ OKKESİM

İSTANBUL, SEPTEMBER / 2014

T.C.
FATİH ÜNİVESİTESİ
BİYOMEDİKAL MÜHENDİSLİK ENSTİTÜSÜ

Wİİ EGZERSİZİNİN PARKİNSON HASTALIĞI ÜZERİNDE Kİ ETKİSİNİN İLGİLİ TREMOR SİNYALLERİ İLE DEĞERLENDİRİLMESİ

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DANIŞMAN
YRD. DOÇ. DR. ŞÜKRÜ OKKESİM

İSTANBUL, EYLÜL / 2014

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FATIH UNIVERSITY

INSTITUTE OF BIOMEDICAL ENGINEERING

Esra ÖZBEK, a **MSc** student of Fatih University **Institute of Biomedical Engineering** student ID 520112017, successfully defended the **thesis** entitled "**EVALUATING EFFECT OF WII EXERCISE ON PARKINSON'S DISEASE-RELATED TREMOR SIGNALS**", which she prepared after fulfilling the requirements specified in the associated legislations, before the jury whose signatures are below.

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It is approved that this thesis has been written in compliance with the formatting rules laid down by the Institute of Biomedical Engineering.

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Director

Date of Submission: 14 August 2014

Date of Defense : 16 September 2014

To my dear father and mother,

This study was supported by Fatih University Research and Development Management Office with the project number of P58011402_B.

ACKNOWLEDGEMENTS

I would like to thank Assist. Prof. Dr. Şükrü OKKESİM, my thesis supervisor, for his inspiration, guidance, motivation and friendly tolerance during my thesis work. I always felt lucky to have been worked with him.

I especially thank to Halil İbrahim ÇAKAR and Mustafa Selman YILDIRIM who are the research assistants of the Biomedical Engineering Institute, for their help in Matlab analysis, and technical support.

I would also like to thank to all my volunteers to help me to collect my data for this research. Also I would like to thank to Gülsen BABACAN YILDIZ, Yıldız AKBAL, Aylin REZVANİ, Eren GÜR, Burcu GÖKŞEN who are the doctors in Bezmialem Vakif University Faculty of Medicine and Hospital for their help in participant selecting and exercise programming.

Furthermore I would like to thank my family and friends who supported me all the time.

September 2014 Esra ÖZBEK

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LIST OF SYMBOLS

Hz	Frequency

ABBREVIATIONS

CNS : Central Nervous System
DBS : Deep Brain Stimulation
DFT : Discrete Fourier Transform
ECG : Electrocardiography
ET : Essential Tremor
FFT : Fast Fourier Transform
FT : Fourier Transform
GPi : Globulus Pallidus İnterna
HP : Highest Peak
MDF : Median Frequency
PD : Parkinson's Disease
PSD : Power Spectral Density
PT : Parkinsonian Tremor
RBD : REM Sleep Behavior Disorder
RSBD : REM Sleep Behaviour Disorder
SD : Standard Deviation
STN : Subthalamic Nucleus
TI : Tremor Intensity
UPDRS : The Unified Parkinson's Disease Rating Scale
WBV : Whole-Body Vibration

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SUMMARY

EVALUATING EFFECT OF WII EXERCISE ON PARKINSON'S DISEASE-RELATED TREMOR SIGNALS

Esra ÖZBEK

Biomedical Engineering Programme

MSc Thesis

Advisor: Assist. Prof. Dr. Şükrü OKKESİM

Parkinson's Disease is a neurodegenerative disorder that is affected loss of dopamine in subthalamic nucleus in basal ganglia. Ratio of PD is 3/1000 in Turkey, and is between 2-5/1000 for United States and west Europe countries. Tremor is a main symptom of Parkinson's Disease.

Tremor is the most common impairment of movement, and it is called as a rhythmic and involuntary oscillation of a body part, caused by reciprocal innervations of a muscle, which leads to repetitive contractions. Prevalence of tremor is 95% in old people, and 5% in young people. Also prevalence of tremor is 350/100.000 around the World, and is 4% in Turkey.

Wii is the game console which is developed from Nintendo Company. These games are based on body balance, and effective on related muscles of human body.

In this study, tremor signals were recorded from patients who are treated in Clinics of Neurology in Bezmialem Vakif University Faculty of Medicine and Hospital. The period of recording was arranged as before Wii exercise, and after Wii exercise to evaluate effect of wii exercise on tremor symptom. Tremor signals were recorded with using accelorimeter from 11 PD patients who are taking same drugs for same duration, and 3 parameters (tremor intensity, highest peak, and median frequency) were calculated. At the end of the study, wii exercise improved just a few subjects' tremor symptoms but there was not observed the same effect on the other subjects' tremor symptoms. In the future study new methods will be used to improve tremor symptom.

Keywords: parkinson's disease, tremor, wii.

FATIH UNIVERSITY - INSTITUTE OF BIOMEDICAL ENGINEERING

ÖZET

Wİİ EGZERSİZİNİN PARKİNSON HASTALIĞI ÜZERİNDE Kİ ETKİSİNİN İLGİLİ TREMOR SİNYALLERİ İLE DEĞERLENDİRİLMESİ

Esra ÖZBEK

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Yüksek Lisans Tezi

Danışman: Yrd. Doç. Dr. Şükrü OKKESİM

Parkinson Hastalığı beynin basal ganglia bölümünde bulunan subtalamik çekirdek tarafından üretilen dopamin miktarının azalması sonucu meydana gelen nörodejeneratif bozukluktur. Türkiye'de görülme oranı 3/1000 iken Avrupa ve Batı Avrupa ülkelerinde bu oran 2/1000 ile 5/1000 arasındadır. Hastalığın en belirgin semptomu tremordur.

Tremor, rutin kasılmaları yöneten kasların, karşılıklı olarak donatılmış sinirlerinin sebep olduğu ritmik ve istemsiz salınımlardır. Tremor yaşlı bireylerde % 95, genç bireylerde ise % 5 oranında görülür. Dünya üzerinde görülme sıklığı 350/100.000, Türkiye'de % 4 şeklindedir.

Wii Nintendo firmasının geliştirdiği bir oyun konsoludur. Bu oyunlar temelde dengeye dayalı olup vücudun ilgili kasları üzerinde etkilidir.

Bu çalışmada, Bezmialem Vakıf Üniversitesi Tıp Fakültesi Hastanesinde Nöroloji Kliniği' nde tedavi görmekte olan hastalardan tremor sinyali kaydedildi. Sinyal kayıt periyodu Wii egzersizinin öncesinde ve sonrasında, Wii egzersizinin tremor üzerindeki etkisini değerlendirecek şekilde düzenlendi. Parkinson hastalığı tanısı almış ve aynı tür ilacı, benzer sürelerde kullanan 11 hastadan ivmeölçer sensör ile tremor sinyali kaydedilerek 3 parametre (tremor yoğunluğu, maksimum spectrum değerinin frekansı, ve orta frekans) hesaplandı. Çalışmanın sonunda, wii egzersizinin sadece bir kaç hastanın tremor semptomunu iyileştirdiği, diğer hastalarda aynı etkiyi yapmadığı görüldü. Gelecekte ki çalışmalarda tremor semptomunu iyileştirici yöntemler kullanılacaktır.

Anahtar kelimeler: parkinson hastalığı, tremor, wii.

CHAPTER 1

INTRODUCTION

1.1 Purpose of the Thesis

Parkinson's Disease (PD) is a common neurodegenerative disorder because of loss of dopaminergic neurons in the basal ganglia of the cerebra [1]. PD is more common over 60 years of age around the World [2]. Also rate of PD for men is higher than that for women [3]. There are approximately 100.000 people are Parkinson's patients. This ratio is 2-5/1000 for United States and west Europe countries. Also in US, 1.5 - 2.5% of people over 70 years are Parkinson's patients. In addition in the United Kingdom, approximately 30-40 patients are diagnosed as PD every day [2]. PD is diagnosed based on the clinical criteria. There is no precisely test for diagnosis of PD, therefore diagnosisis is generally based on the main motor features in clinic. There are rating scales to evaluate motor disorders and disability in patients with PD. One of the these rating scales is Hoehn and Yahr scale which is frequently used to compare group of patients in clinics, and the other scale is The Unified Parkinson's Disease Rating scale (UPDRS). UPDRS is the most well accepted scale for evaluating disability and disorder [4]. The major symptoms of Parkinson's Disease are tremor, bradykinesia, rigidity, and postural disturbance [2]. There are several non-motor impairments such as dysautonomia, olfactory dysfunction, sleep disorder, and mood disturbances in PD. Also premotor symptoms in PD include constipation, loss of smell, sleep disturbances, mood disturbances like depression, anxiety, restless-legs syndrome, pain, apathy, and fatigue [5]. In addition to premotor symptoms, researchers have determined different premotor symptoms such as urinary problem, affective changes, cognitive changes, weight loss, psychosis, and dementia in premotor phase of PD [6].

Tremor is the most common movement disorder of PD that is involuntary oscillation of body parts. There are differences between tremor and other involuntary movement disorders, such as chorea, athetosis, and ballism, by its repetitive and stereotyped movements, with regular frequency and amplitude. Tremor is classified by two systems. The first system based on its form of occurance (static or an action). Also second one is based on its causes (physiological or pathological). Parkinsonian tremor (PT) is type of static tremor that is seen during resting and also essential tremor (ET) is type of action tremor which is seen during action. The physiological tremor occurs in all healthy human beings due to happiness, stress, muscular fatigue, anxiety, fright, and it can rise with the use of chemical substance and consumption of alcohol [2].

Physical therapy techniques are useful for treatment of balance, mobility, and gait following neurological disorder. In clinic, video game consoles such as the Nintendo Wii Fit are used as rehabilitation tools [7]. Wii is a game console which was developed by Nintendo Company. Main principle of Wii is balance. Additionally the game is used to improve human posture [8].

The aim of this thesis is to search out effect of Wii exercise on PT. Tremor signals was recorded by accelerometer from 11 (7 Female, 4 Male) PD patients who diagnosed by neurologist in Bezmialem Vakif University Faculty of Medicine and Hospital, Clinics of Neurology. Subjects have taken Wii exercise programme for nine weeks after who were diagnosed and accepted for study. They have played three different games for each train and each of these games durations were 10 minutes. Tremor signals were recorded before Wii exercise program and at end of the exercise programme. xyzPlux Accelerometry Sensor of Plux- Engenharia de Biosensores, Lda. was used for data acquisition and the tremor signals were sampled at 1000 sampled/second. The electrodes were placed on the metacarpophalangeal joints on the index fingers both of right and left hands and signals were recorded in 3 cases (hands were on the table, hands were in free fall, and during task) and duration of each of cases was 3 minutes.

In the literature there are three parameters to analysis tremor such as tremor intensity in time domain (TI), highest peak (HP), and median frequency (MDF) in frequency domain [9]. Parameters were calculated by Fast Fourier Transform (FFT) method and Power Spectral Analysis was applied to spectrum of the tremor signals. Also calculated parameters were compared statistically.

1.2 Hypothesis

Tremor is the most common motor disturbance of PD and PD patients suffer from tremor in their daily lives. Physical therapy is used to improve tremor, balance, gait, postural instability, and other neurological injury. Nintendo Wii video game console is used as rehabilitation tool for treatment of some diseases such as stroke and PD. End of the exercise programme, possitive effects (decreasing tremor intensity, improving postural instability, etc.) of Wii exercise can be seen on patients with PD and can be evaluated according to related tremor signals.

1.3 Literature Survey

There are lots of studies about PD in literature. The premotor phase of PD was published by Y.Compta *et al*., they assumed that a variety of symptoms can precede the classical motor disorders of PD. Also, it can be defined as the premotor phase of the disease when these symptoms increase. As a result they hypothesized that the premotor symptoms of PD are constipation, loss of smell, sleep disturbances such as REM sleep behavior disorder (RBD), and mood disturbances like depression. They discussed diagnostic and therapeutic implications linked to developed recognition of these premotor symptoms [5]. Before the motor symptoms were researched and published by Tanya Gurevich *et al*., they reviewed premotor disturbances and their contribution to the clasification of the pathophysiologic processes of PD, and discussed the implications for treatment of the disease. The manifestations of PD were classified in 3 stages: premotor clinical manifestations of PD, early motor phase, late stages. According to Tanya Gurevich *et al*., premotor clinical manifestations of PD include olfactory dysfunction, sleep associated features, urinary problem, affective changes, cognitive changes, weight loss, and pain complains. Early motor phase includes resting tremor, bradykinesia, and rigidity. Also, depression, apathy, psychosis, and dementia are features of late stages. They assumed that the identification of premotor disturbances will allow an earlier diagnosis of the PD [6].

There are several studies about symptoms of PD. One of these symptoms is tremor. According to Paulo Henrique *et al*. tremor is the most extensive disturbance and differs from other impairments by its repetitive, with regular frequency and amplitude. There is no information about causes of tremor and its main characteristics. Paulo Henrique *et al*. published the methods which are generally used in measurement and analysis of tremor. They encountered the difficulties in this study for the recognition of methodologies that allow an important advance in the research of tremor. One of these methods is UPDRS that is the most common and favorable clinical method. Also accelerometry, electromyography, and the spinogram are main methods commonly used to measure the tremor in laboratory. In addition, some analysis methods are used to evaluate of the data such as, Fourier Transform (FT), and FFT. They observed that, there is no an ideal method for the study of tremor signal [2]. Fluctuations in tremor and respiration in patients with PD were researched and published by Anne Beuter *et al*., they evaluated results of fluctuations in tremor of PD patients. They tested 2 patients with fluctuations in tremor and 1 patient with no fluctuations in tremor. Also they recorded blood pressure, electrocardiography (ECG), respiration, and tremor for 5 minutes in relax position with eye closed, performing substractions mentally or listening to a story. Abrupt transitions were recorded from patients in both of tremor and respiration. No fluctuation was observed in either respiration or tremor in patient with no fluctuation. Aim of this study was to identify the qualitative changes occuring in tremor and respiratory in PD patients [10].

Accelerometry-based studies were applied to patients. Body vibration was studied and published by Hugo Silva *et al*.. The purpose of their study was to identify the vibration delivered by a whole-body vibration (WBV) exercise platform and quantify the acceleration transmissibility throughout the body while doing different WBV exercises. There was accelerometry-based setup for evaluating vibration frequencies and suitable magnitudes both at the side-alternating vibration platform and on multiple anatomic lanmarks of the participant’s body. They studied with 14 subjects who participated a sequence of four different exercises. The results showed that vibration induced during the body movement. Also, different exercises seem to effect the vibration transmissibility to some extent [11].

Some experiments were done to evaluate tremor characteristics by measured some parameters. Zsuzsanna Farkas *et al.* researched the asymmetry of tremor intensity, frequency and frequency dispersion of PT and ET tremor with accelerometry. Signals of the more and less tremor of hands were evaluated statistically. They found that tremor intensity was importantly asymmetric not only in PT but also in ET, while frequency and frequency dispersion were symmetric in ET but asymmetric in PT. They concluded that bilateral assessment of frequency related tremor features may be used to seperate ET and PT, and provides further details on the central mechanism of tremor generators [9]. In the another study A. Beuter *et al.* researched methods of formulating signs to characterize abnormalities in tremor with using computerized tremor analysis systems. Identifying of amplitude, frequency, and “harmonicity” were considered as well as how to combine several such features into a single sign to seperate abnormal tremor and normal tremor effectively. The methodological issues discussed here should be of interest to researchers and clinicians working with tremor in general and to both users and developers of computer tremor analysis systems [12].

Priya V. Mhatre *et al.* used the Nintendo Wii Fit video game to assess the effect of exercise training on balance and gait in adults with PD. They studied with ten subjects with PD who participated 3 times per week for 8 weeks by practicing 3 different Wii balance board games (marble tracking, bubble rafting, and skiing) adjusted for their individualized function level. The subjects made effort for 10 minutes per game, a total of 30 minutes training per case. They conclude that an 8-week exercise training class by using the Wii Fit balance board improved selective measures of balance and gait in PD patients. However, there were no important changes in mood or confidence regarding balance [13].

Physical therapy techniques are useful for treatment of balance, mobility, and gait following neurological disorder. In clinic, video game consoles such as the Nintendo Wii Fit are used as rehabilitation tools [7]. Wii is a video game console which was developed by Nintendo Company. Main principle of Wii is balance. Additionally the game is used to improve human posture [8].

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Accelerometry Sensor of Plux-Engenharia de Biosensores, Lda. was used for data acquisition and the tremor signals were sampled at 1000 sampled/second. The electrodes were placed on the metacarpophalangeal joints on the index fingers both of right and left hands and signals were recorded in 3 cases (hands were on the table, hands were in free fall, and during task) and duration of each of cases was 3 minutes.

In the literature there are three parameters to analysis tremor such as tremor intensity (TI), highest peak, and median frequency in time domain and frequency domain [9]. Parameters were calculated by FFT method and Power Spectral Analysis was applied to tremor signals. Also calculated parameters were compared by statistical and evaluated.

CHAPTER 2

BACKGROUND

2.1 Parkinson's Disease

The human motor system controls the human posture, force and movement. Motor system includes that central motor system and motor units. The figure about structure of motor system is presented in Fig. 2.1 (a). Each motor unit consists of a motor neuron, multiple branches of its axon, and the muscle fibers that it innervates. Cerebra includes several cortical parts. These are the premotor cortex, motor area, and the associated regions of the cortex. The signal pulses come from these regions, from cerebellum, and from the basal ganglia then neurons of the primary motor cortex are affected. The output signals from the primary motor cortex affect the inter-neurons and motor neurons in the spinal cord. This system controls the muscle activity [14].

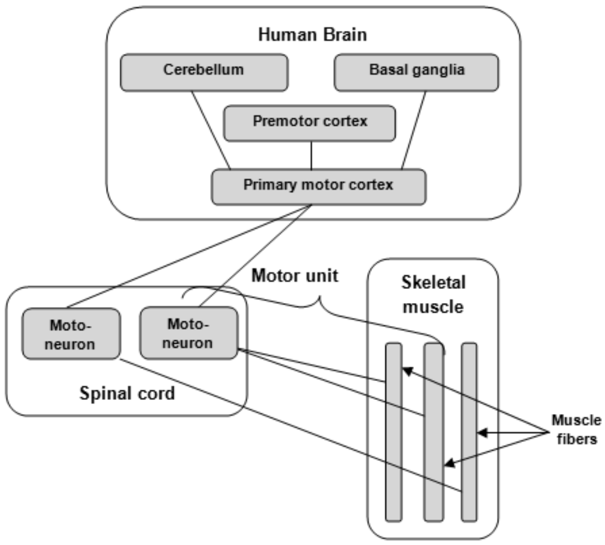


Figure 2.1 Motor system [14]

The brain is a complex organ in a vertebrate's body that is present in central nervous system. For a typical human cerebra, the cerebral cortex contains approximately 15-33 billion neurons. Each neuron is connected by synapses to other neurons. These neurons communicate with the other neurons by protoplasmic fibers called axon [15]. An axon can make lots of synaptic connections with other cells. Transmit signal arrives at a synapse from a neuron to another target neuron by chemical substance called neurotransmitter [16]. There are many types of neurotransmitter. Major neurotransmitters are amino acids (glutamate, aspartate, D-serine, γ-aminobutyric acid (GABA), glycine), monoamines and other biogenic amines (dopamine, serotonin, norepinephrine (noradrenaline), histamine, epinephrine), trace amines (phenethylamine, tyramine, 3 iodothyronamine, *N*-methylphenethylamine, Octopamine, tryptamine, N,N-Dimethyltrytamine), peptides (somatostatin, substance P, cocaine and amphetamine regulated transcript, opioid peptides), and acetylcholine, adenosine, anandamide, nitrit oxide, etc. [17]. Dopamine is a hormone that plays significant roles in the human brain and body such as motor control, motivation, arousal, and cognition. In the human brain dopamine behaves as a neurotransmitter. There are 400.000 dopaminergic neurons (neurotransmitter) in the human brain [18]. Dopaminergic cells were first determined in 1964 by Annica Dahlström and Kjell Fuxe [19]. Dopamine is secreted by substantia nigra that is a small midbrain region and component of the basal ganglia. Large amount of dopaminergic neurons are found in a part of this structure and they affect striatum, globus pallidus (GPi), and subthalamic nucleus (STN) all of which are components of basal ganglia and they are affected in motor control [20]. The basal ganglia (basal nuclei) are multiple subcortical nuclei and located at the forebrain. The structure of basal ganglia is shown in Fig. 2.1 (b). Basal ganglia are connected with cerebral cortex, thalamus, brainstem, and other regions of cerebra. Also, basal ganglia play the important role of control of voluntary motor movement, procedural learning, routine daily behaviour such as eye movement, cognition, etc. [21].

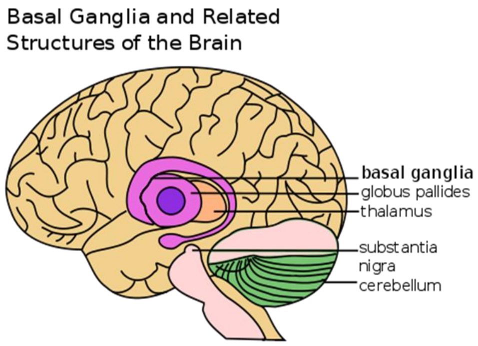


Figure 2.2 Basal ganglia structures of the brain [41]

Neurodegenerative disorders are defined by researchers as process of certain biochemical changes, which in turn lead to others. Results of these biochemical changes are seen in clinically and pathologically [22].

PD is a chronic progressive neurodegenerative disease [14]. PD was determined in an article “An Essay on the Shaking Palsy” by English Doctor James Parkinson in 1817 [2]. PD affects 0.3% of around the World and 1% of people over 60 years of age. The incidence of PD in south-western Finland was 166/100.000 persons in year 1992 [14]. In North America over 1 million people was PD patient in year 1998 [23]. The prevalence of PD patients is 150-200/100.000 people over 70 years of age in the United States. In the United Kingdom, approximately 30 to 40 people are diagnosed every day. The number of patients increases by increasing age. 1% of people over 65 years of age are PD patients, and this rate is doubles among the society over 85 years of age [2]. The basic phenomenon of PD is loss of dopaminergic neurons in the substantia nigra in the basal ganglia of the brain and Lewy bodies (LB) are seen in degenerating neurons [6]. Extrapyramidal system is controlled by the dopaminergic neurons that the mechanism of the input from the cortex to the striatum and returns it through the thalamus back to the cortex in healthy person. In PD patient, the control of this system is damaged and the feedback from the striatum to the cortex is modified. The disturbances in the function of basal ganglia control the motor symptoms of PD [14].

However the exact cause of PD is stil undefined. There are several risk factors for PD that include genetic factors, environmental risk factors, age, and family history [14].

There are several clinical manifestions in PD that are defined as motor symptoms and non-motor symptoms. The cardinal motor signs are tremor, bradykinesia, rigidity, and postural instability that are seen in Fig. 2.1 (c) [14]. Also, non-motor features are observed in PD such as dysautonomia, olfactory dysfunction (loss of smell), sleep disorder, and mood disturbances, constipation, restless-legs syndrome, pain, apathy, and fatigue [5]. In addition to premotor symptoms, researchers have determined different premotor symptoms such as urinary problem, affective changes, cognitive changes, weight loss, psychosis, and dementia in premotor phase of PD [6].

Tremor is the most common movement disturbance of PD. It is defined as involuntary, rhythmic and oscillatory movements of body parts. Bradykinesia is slowness at initiating and leading movement and it causes difficulties with planning in daily living.

The rate of the bradykinesia is 77-98% of PD patients. Rigidity is determined by involuntary increase in the muscle tone of the limb that is observed during or before movement. There are 89-99% of PD patients suffer from rigidity. The other motor symptom is postural instability that because of loss of postural reflexes and it seen in late stage of PD [14].

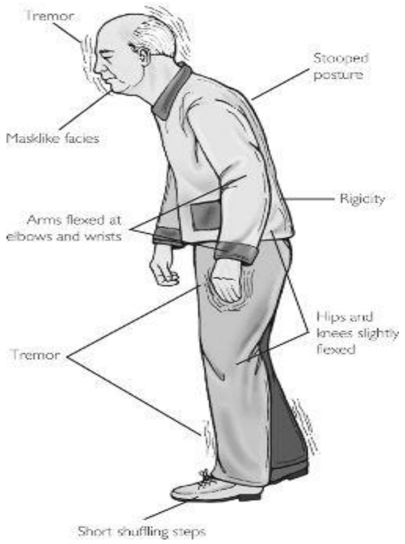


Figure 2.3 Motor symptoms of PD [42]

Dysautonomia is a well-known non-motor symptoms of PD that appears in the advanced stages of PD. In some instances side effects of treatment can play a role in increasing of this sign. Generally, in early phase of the disease PD patients suffer from olfactory dysfunction such as damage in odor detection, identification, and determination [5]. The olfactory bulb includes dopaminergic neurons and olfactory loss is related to disturb of dopaminergic cells [6]. Patients with PD suffer from sleep related disorders that include insomnia, parasomnia, excessive daytime sleepiness. It has been estimated 60-98% patients with PD suffer from sleep disorder [5]. Mood disturbances such as depression and anxiety are seen in PD. The incidence of depression is 40% of PD patients at the early stage of the disease. Also, depressive signs in PD are defined by relative lack of guilt, shame, or sorrow when compared with depression in society [5]. Pain is the other non-motor disturbance of PD that is related to muscle rigidity and bradykinesia. Apathy appears in late stage of disease taht is called much more mental disturbances. Urinary problems are observed in PD that is affects 30-70% of PD patients. Urination problems in PD can be associated by bradykinesia and difficulty getting out of bed and mobilizing at night, contributing to sleep disorder. Affective changes are seen in PD patients like depression. In fact that this manifestion occurs in pre-motor phase but sometimes neurologists ignore this situation. Cognitive deficit is another non-motor disturbance of PD that is similar to complains in early phase of Alzheimer's Disease. The estimated causes of this complain memory impairment and cortical depositon of LB. Weigth loss is observed in PD patients as other several neurodegenerative disorder. It can be related to increased metabolic and physical activity. Psychosis is observed in patients with PD at the advanced stage of PD. Hallucinations are reported from patients like imagining that people around them. Following of this disturbance decreased consciousness and dementia are seen. The treatment of psychosis is difficult in PD patients. Common neuroleptics causes increasing of PD [6]. At advanced phase of PD patients suffer from severe dementia [6].

2.2 Diagnose and Treatment Methods

In clinics there is no certain test for diagnosis of PD [4]. The diagnosis of this disease is based on the presence of clinical symptoms and on the response to anti-parkinsonian drugs. Diagnostic accuracy is increased by several diagnostic criteria. Imaging tecniques such as the positron emission tomography (PET), single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI) are used for diagnosis of PD [14]. On the other hand rating scales are used for the evaluation of motor impairment of PD patients. The Hoehn and Yahr scale is commonly used to diagnose PD patients according to stages of scale (stage 0: no signs of disease to stage 5: bedridden unless assisted) [4]. Also the most widely used scale is Unified Parkinson's Disease Rating Scale (UPDRS). UPDRS includes four parts: I) Mentation, Behavior and Mood, II) Activities of Daily Living, III) Motor Examination, and IV) Complications of Therapy [14]. Also, according to scale values from 0 to 4 are evaluted depending on the seriousness: 0-without problems; 1- minimal problems; 2- mild problems; 3- moderate problems; and 4- severe problems [2]. The motor examination part of this scale may be used to score numerically the intensity of most important motor symptoms of PD [14].

In PD, there are two treatment procedures as medication and surgery method. The manifestions can be relieved with anti-parkinsonian medication that inhibit the breakdown of dopamine in the cerebra. There are several types of drugs for decreasing motor disorders of PD and the most effective drug group is the levodopa (L-DOPA)

[14]. L-DOPA cross to brain-barier system by the active transport mechanism for large neutral amino acids. Thus, it leads motor complications. The dose and using time of drugs are depend on the patients [24]. A long-term using of anti-parkinsonian drug patient can be worse [14]. The other treatment method is stereotactic surgery method whic is called deep brain stimulation (DBS) (Fig. 2.3) that is applied to patient when medication is not enough for decreasing the disturbances. DBS is favorable for reducing tremor, bradykinesia, and rigidity in PD. DBS device includes that implanted pulse generator, connecting wire, and one or two electrodes. Electrodes are located in the subthalamic nucleus (STN) or globulus pallidus interna (GPi). The success of DBS method related with certain locations of the stimulation electrodes [14]. DBS treatment technique is effective on the cognitive functions. According to M. Jahanshahi *et al*. DBS surgery technique provides improving of executive functions but N. Chastan *et al.* searched out that despite activity of daily living and parkinsonian motor disfunctions are improved by DBS, cognitive functions are decreased 5 years after surgical operation [25] [26]. There are several studies about this stituation.

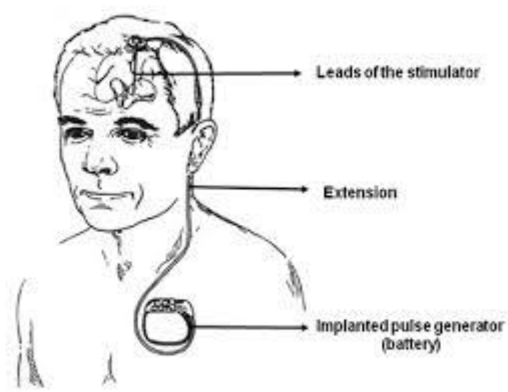


Figure 2.4 Deep brain stimulation mechanism [43]

2.3 Tremor

Tremor is the most common impairment of movement, and it is determined that rhythmic and involuntary oscillation of the body part. It can vary in frequency and amplitude so it is differs from other involuntary movement disorders according to regular frequency and amplitude. There are three commonly tremor types such as ET, PT, and physiological tremor that appear in patients. ET is observed in hands and intensity of ET decreases during voluntary movements. The ET affects one million people in the United States. In some studies the incidence of essential tremor was 4%

over 40 years of age in Turkey, 5-6% in Finland for same age group. In elderly patients, ET affects the upper limb (95%), the head (34%), the lower limbs (20%), the voice (12%), the face (5%), and the trunk (5%). In some intances, this type of tremor is visible during action. The most advanced stages static tremor appears in patient, so separation of ET and PT can be difficult. PT is more visible in resting position, but may be it appears in the posture and may be confused with ET. Also the physiological tremor is normal and appears in all healthy person. This type of tremor only happens in several cases such as stress, muscular fatigue, anxiety, fear and it increases with using chemical substances and alcohol [2].

Tremor is classified in two systems. The first system is based on its form of occurrence (static or action), and the other system is based on its causes (physiological or pathological) [2].

The static tremor happens during resting position and it usually disappears during movement or action begins. The action tremor appears during a voluntary movement. It includes postural, isometric, and kinetic types of tremor. According to some researchers the task-specific tremor and intentional tremor are types of action tremor. The postural tremor is observed in a body part which is in against position to the gravity. The isometric tremor happens when there is a muscular contraction against a stationary object. The kinetic tremor occurs only during the action with the affected body part such as limb. The task-specific tremor happens during the specific task such as writing. In addition, intentional tremor increases intensity when the person approaches a certain target who wants to reach [2].

2.4 Tremor Signals

Tremor is a major symptom of PD. In literature there are many descriptions and classifiying types of tremor depend on the frequency and amplitude. Generally an increase in tremor amplitude especially on one side of the body has been used as an indication of pathology, but early stages of neurologic disorder are not necessarily idenficated by an increase in tremor amplitude. In addition, tremor frequency appears more stable over time than amplitude measures [27]. Typically tremors are unilateral happen at a frequency about 4-6 Hz [4]. Normal physiologic tremor is identified at a frequency between 8 to 12 Hz that depends on the mechanical resonance frequency of the related body part. PT is characterized in the 4-6 Hz range and ET appears in normal range and it depends on the age. The place of tremor recording is more significant. If tremor signals are recorded from metacarpophalangeal joint, the mechanical resonance oscillation of the index finger is about 17 Hz. If it is recorded from the wrist, the mechanical resonance oscillation is the 8 to12 Hz [27]. So types of tremor can be seperated from each other according to frequency range.

2.5 Research on Tremor Signal Processing

Some experiments were done to evaluate tremor characteristics by measured some parameters. The asymmetry of tremor intensity, frequency and frequency dispersion of PT and ET were investigated using accelerometry by Zsuzsanna Farkas *et al.*. Data of the more and less trembling hands were statistically elaborated. According to their founding tremor intensity was significantly asymmetric not only in PT but also in ET, while frequency and frequency dispersion were symmetric in ET but asymmetric in PT. They conclude that bilateral evaluating of frequency related tremor parameters may be used for differentiation between ET and PT, and provides further details on the central organization of tremor generators [9].

In the another study A. Beuter *et al.* considered methods of formulating indexes to identify abnormalities in tremor appropriate for computerized tremor analysis systems. Characterization of amplitude, frequency, and "harmonicity" were considered as well as how to combine several such characteristics into a single index to discriminate normal from abnormal tremor effectively. The methodological issues discussed here should be of interest to researchers and clinicians working with tremor in general and to both users and developers of computer tremor analysis systems [12].

Several parameters were evaluated to determine characteristics of tremor types. A. Beuter *et al.* tested 21 PD patients that previously diagnosed and 30 neurologically healthy subjects. Tremor signals were recorded from both of two hands of subjects for two procedures. First, rest tremor and postural tremor with no visual feedback. Second, postural tremor with visual feedback. Different tremor types of tremor were recorded from subjects, and from these tremor time series velocity and acceleration data were obtained. Amplitude (tremor intensity) and seven frequency domain parameters (dispersion about median frequency, harmonic index, center of mass frequency concentration, highest peak, median frequency, proportional power in the 4- to 6-Hz range, proportional power in the 7- to 12- Hz range) were calculated for each recording and each discriminating power was compared. The most reliable, independent, favorable, and discriminative characteristics were determined [27].

2.6 Wii Exercise and It's Role in Physical Therapy

Physical therapy techniques are used for treatment of balance, mobility, and gait following neurological disorder. In clinic, video game consoles such as the Nintendo Wii Fit are used as rehabilitation tools [7]. Wii is a video game console which was developed by Nintendo Company. Main principle of Wii is balance. Additionally the game is used to improve human posture [8]. Some studies have shown that using of video games can provide improving balance impairment [7].

CHAPTER 3

MATERIALS AND METHODS

This chapter is about information of participants, the procedure of research, the measurement system used in this study and signal processing methods.

Before selecting subjects, ethical approval was taken from Bezmialem Vakif University Faculty of Medicine and Hospital. Ethical approval code is 71306642/050-01-04/241.

In this study, subjects were selected with Associate Professor Gülsen BABACAN YILDIZ, Assistant Doctor Eren GÜR (Clinics of Neurology), Associate Professor Aylin REZVANİ, and Assistant Doctor Yıldız AKBAL (Clinics of Physical Therapy and Rehabilitation). Also, Wii exercises were programmed by Assistant Doctor Yıldız AKBAL.

3.1 Participants

PD patients (N=11; 7 female and 4 male) were diagnosed by Associate Professor Gülsen BABACAN YILDIZ in Clinics of Neurology in Bezmialem Vakif University Faculty of Medicine and Hospital. Participants were taking same drugs for same duration. Informations about patients as their dominant hands, tremor sides, disease durations, loss of smells, constipations, and rem sleep behaviour disorders (RSBD) are shown in Table 3.1.

Table 3.1 Demographic informations of the subjects

Subject	Gender	Dominant hand	Tremor side	Disease duration	Loss of smell	Constipation	RSBD
S 1	F	R	L	11 years	Yes	Yes	No
S 2	M	R	R	3 years	No	Yes	Yes
S 3	F	R	L	10 years	No	No	No
S 4	M	R	R	7 years	Yes	No	Yes
S 5	F	R	R	1,5 years	Yes	No	Yes
S 6	F	R	L	5 years	No	No	No
S 7	F	R	L	2 years	Yes	Yes	No
S 8	F	R	L	2 years	No	Yes	Yes
S 9	M	R	L	2 years	No	No	Yes
S 10	M	R	L	4 years	No	No	No
S 11	F	R	R	10 years	Yes	Yes	Yes

3.1.1 Inclusion and Exclusion Criteria

Subjects were selected from PD patients according to several criteria. Subjects were selected by Clinics of Neurology and Clinics of Physical Therapy and Rehabilitation.

1) Inclusion Criteria: Subjects were accepted for study according to these criteria.

- Parkinson Disease patients,
- Has not been in any Wii exercise or rehabilitation programme.

2) Exclusion Criteria: Subjects were not accepted for study who have got these criteria.

- Changeable medical treatment during the study,
- Uncontrollable orthostatic hypotension,
- Symptomatic coronary artery disease,
- Lower body fractured before 6 months of study,
- Orthopedic and neurological dysfunction,
- Psychosis and uncontrollable depression,

- Severe dyskinesia induced by L-DOPA,
- Severe visual disorder
- Patients without dyskinesia.

3.2 Wii Exercise Programme

Subjects have taken Wii exercise programme for nine weeks after who were diagnosed and accepted for study. They have played three different games (Fig. 3.1).

1. One of these games was related to lower body performance. Patients moved as step on the Wii Fit balance board (Fig. 3.1 (a)).

2. Other game was related upper body performance. Subjects stood on the Wii Fit balance board. They were sensible for ball which appeared on the monitor and they butted to ball (Fig. 3.1 (b)).

3. The last game was related to upper body extremities performance. Subjects held the Wii remote by one hand and Nunchuck controller by the other hand. Then they moved like play boxing (Fig. 3.1 (c)).

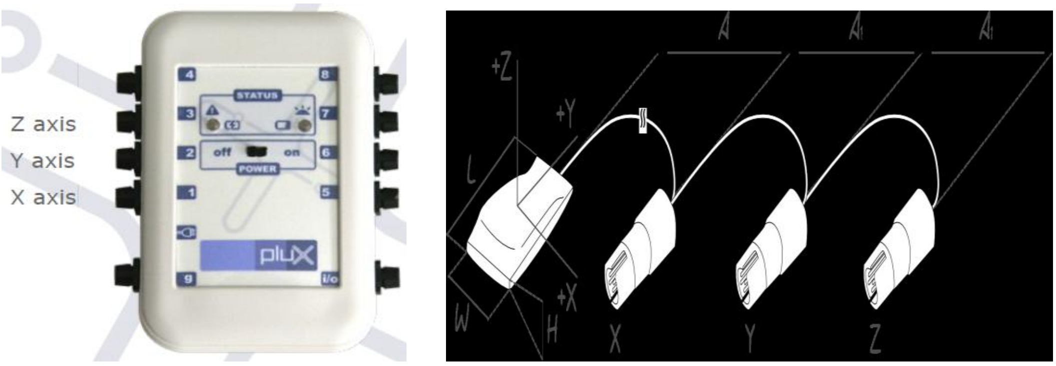
(a) (b) (c)

Figure 3.1 Wii games were used for study as walking (a) [44], butting to ball (b) [45], boxing (c) [46]

Each of these games durations were ten minutes, so total duration of a session was thirty minutes. Also subjects attended this exercise for two times per a week, so they played these games for 18 sessions.

3.3 Tremor Signal Recording

Tremor signals were recorded before Wii exercise programme and at end of the exercise programme. xyzPlux Accelerometry Sensor (Fig. 3.2) of Plux-Engenharia de Biosensores, Lda. was used for data acquisition and the tremor signals were sampled at 1000 sampled/second. The electrodes were placed on the metacarpophalangeal joints on the index fingers (Fig. 3.3) both of right and left hands and signals were recorded in 3 cases (hands were on the table, hands were in free fall, and during task) and duration of each of cases was 3 minutes. Recording positions are seen in Fig. 3.4.



(a) (b)

Figure 3.2 3 axial (b) accelerometer (a) was used for data recording [47]

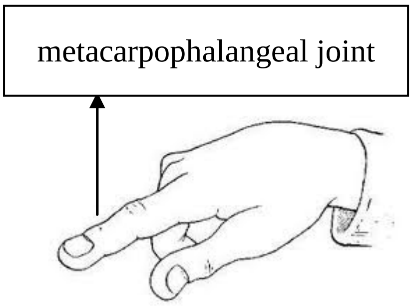


Figure 3.3 Electrode placed at the metacarpophalangeal joint [48]

(a) (b) (c)

Figure 3.4 Data recording cases

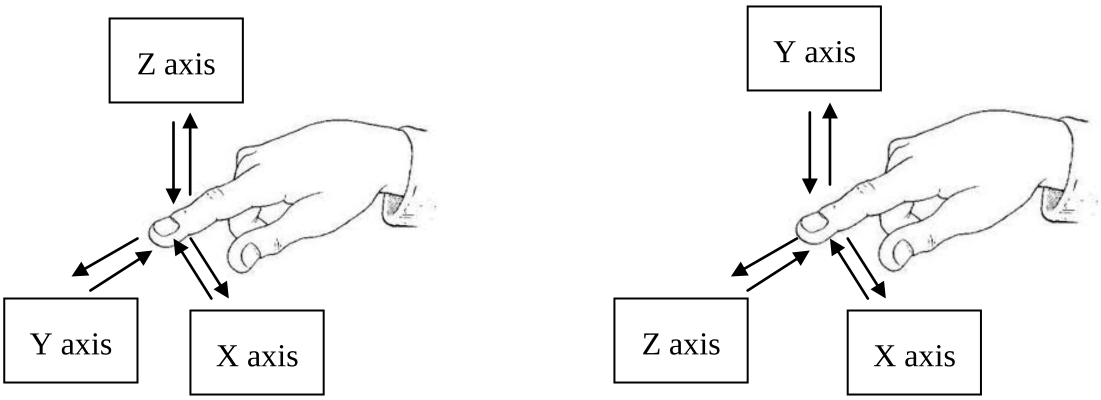
Each recording case was entitled such as A1, A2, and A3.

A1: The case that hands were on the table (Fig. 3.4 (a)).

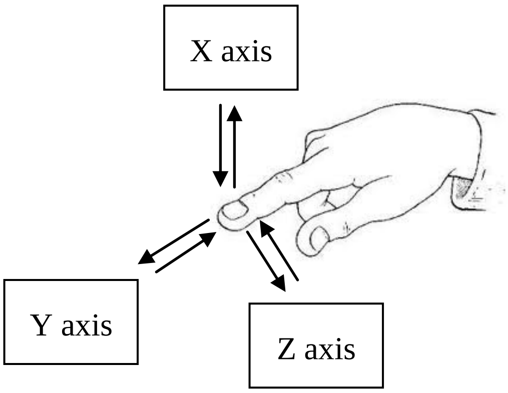
A2: Hands were in free fall position in this case (Fig. 3.4 (b)).

A3: During specific task (Fig. 3.4 (c)).

Axial direction changed according to recording cases. For A1 recording case, X axis was sensible for right and left motion, Y axis was sensible for forward and backward motion, also Z axis was sensible for upward and downward motion (Fig. 3.5 (a)). For A2 recording case, X axis was sensible for right and left motion, Y axis was sensible for upward and downward motion, and Z axis was sensible for forward and backward motion (Fig. 3.5 (b)). Lastly, for A3 recording case, X axis was sensible for upward and downward motion, Y axis was sensible for forward and backward motion, also Z axis was sensible for right and left motion (Fig. 3.5 (c)).



(a) (b)



(c)

Figure 3.5 (a) (b) (c) Axial directions related to recording cases

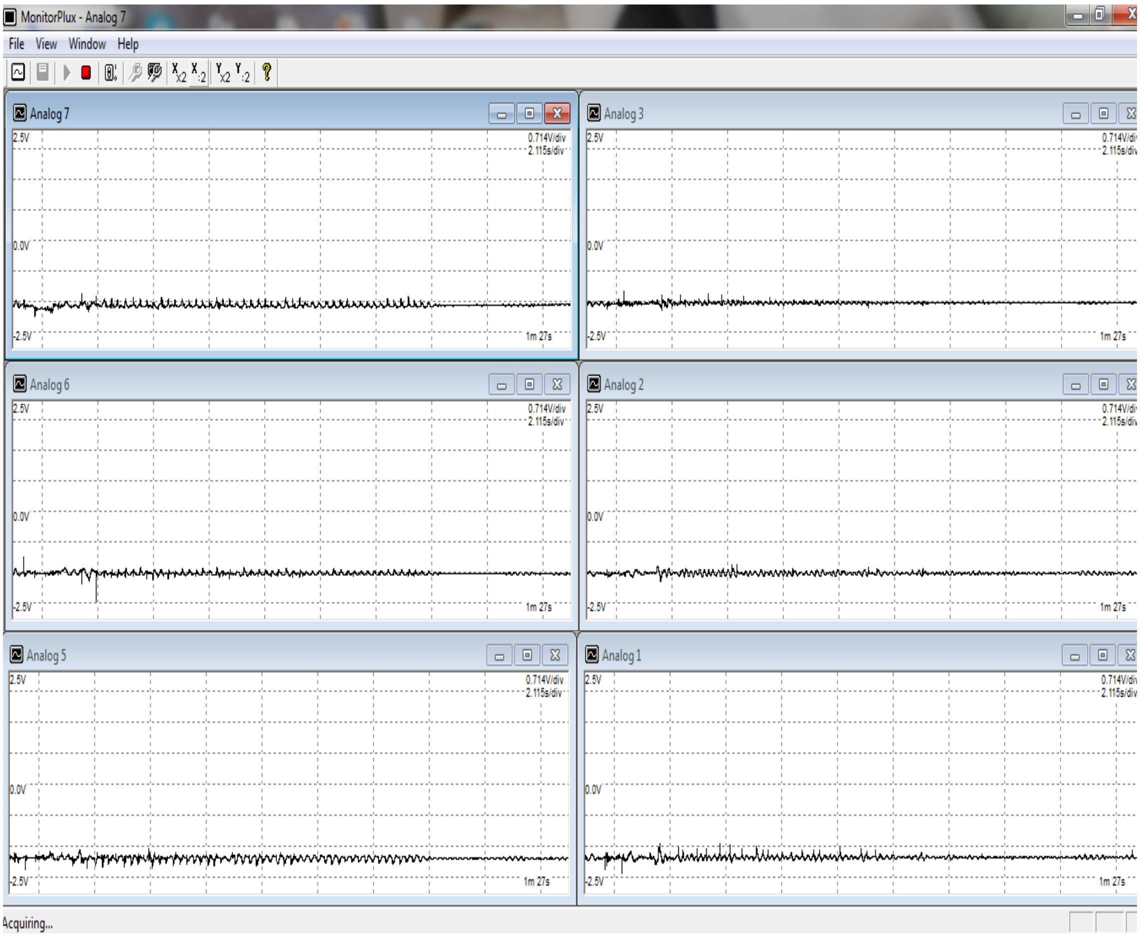


Figure 3.6 Screen view of raw data during recording

During the recording MonitorPlux programme was used to see raw data. Right X axis was showed window 1 and left X axis was showed window 5, right Y axis was showed window 2 and left Y axis was showed window 6, right Z axis was showed window 3 and left Z axis was showed window 7 (Fig. 3.6).

3.4 Analyzing of Tremor Signals

3.4.1 Fast Fourier Transform and Power Spectral Density for Spectral Analysis

For all of the trains, the recording signals were transformed in digital signals sequences and stored in a computer for following analysis. FFT is a highly efficient algorithm for computing the Discrete-Fourier transform (DFT) of a time series [28]. FFT method is used more, regardless of the signal type and specific results are obtained with using FFT method. FFT algorithms plays an important role in the widespread use of digital signal processing in a several applications like telecommunications, medical devices, radar, etc. [29]. FT of a signal can given with Equation (3.1) below.

The Power Spectral Density (PSD) is the most useful function to used frequency domain of tremor signals. PSD variables of signals was calculated by using Welch method.

$$x(w) = \int_{-\infty}^{\infty} x(t) e^{-jwt} dt \tag{3.1}$$

Autocorrelation function $R_x(t)$ was given in Equation (3.2).

$$R_x(\tau) = \frac{1}{T} \int_{0}^{T} x(t).x(t+\tau) dt \tag{3.2}$$

The PSD of a signal is obtained to be get the FT of the signal's autocorrelation function that can given in Equation (3.3).

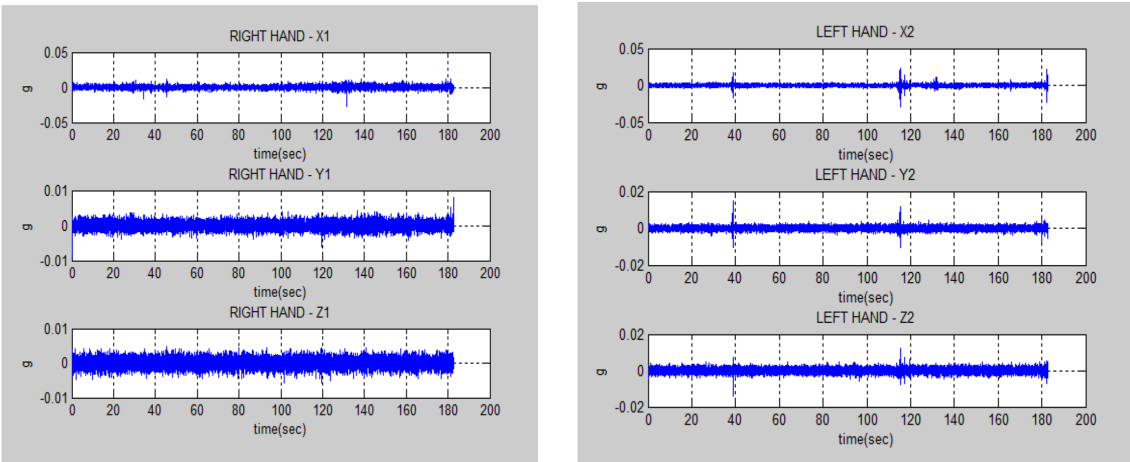
$$\Phi_x(w) = \int_{-\infty}^{\infty} R_x(\tau).e^{-jwt} d\tau \tag{3.3}$$

The Power spectrum shows power density in the "w" frequency and measures the signal's power component in each frequency. All of the frequency components' PSD integral which are create the signal, provide to be calculated the total power (Equation 3.4).

$$P = R_x(0) = \frac{1}{2\pi}\int_{-\infty}^{\infty}\Phi_x(w)dw \qquad (3.4)$$

3.4.2 Features Computed from Tremor Signals

Before features computed from tremor signals, obtaning data was filtered by using IIR Butterworth filter and signals was drew by MATLAB (The MathWorks, Inc). Drawn tremor signals for right and left hands were showed in Fig. 3.14.



(a) (b)

Figure 3.7 Filtered tremor signals for (a) right hand and (b) left hand

In this study one of the three parameters was calculated in time domain and others were calculated in frequency domain by using some analyzing methods.

1. Tremor intensity (TI)
2. Highest peak (HP)
3. Median frequency (MDF)

3.4.2.1 Tremor Intesity (TI)

Tremor intensity is used in amplitude analysis. This feature is determined by root mean square (RMS) of acceleration recorded data. Frequency band of tremor intensity is between 0.9 and 15 Hz. Larger values shows that more intense tremor [11]. The mathematical expression for the RMS function can given in Equation (3.5).

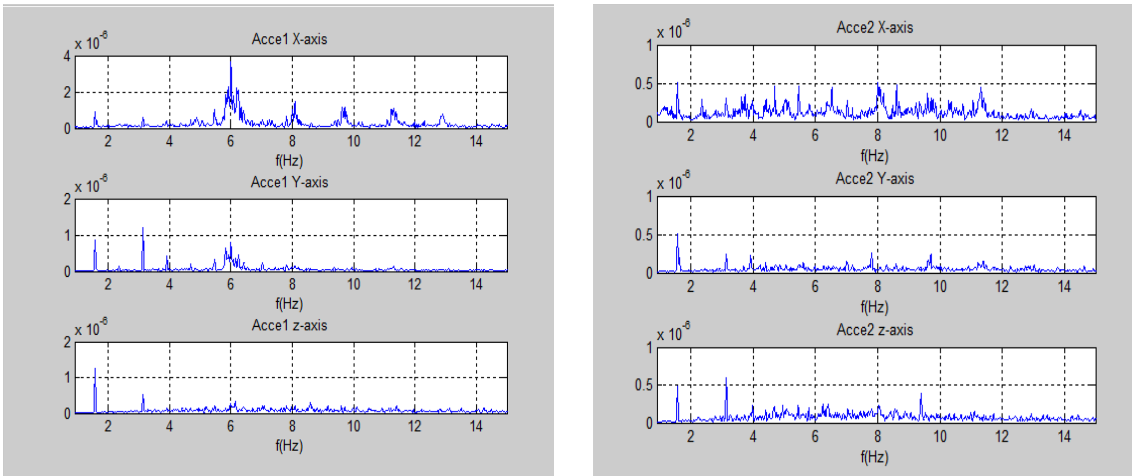
$$RMS = \sqrt{\frac{1}{K}\sum_{n=1}^{K} s_n^2} \tag{3.5}$$

TI was calculated using Equation (3.4), where

K: the number of samples,

S_n: the value of the n-th segment of array.

RMS graphs of tremor signal for right and left hand was showed in Fig. 3.8 (a) (b). Acce1 represent the sensor which was located on index finger of right hand and Acce2 represent the other sensor which was located on index finger of left hand.

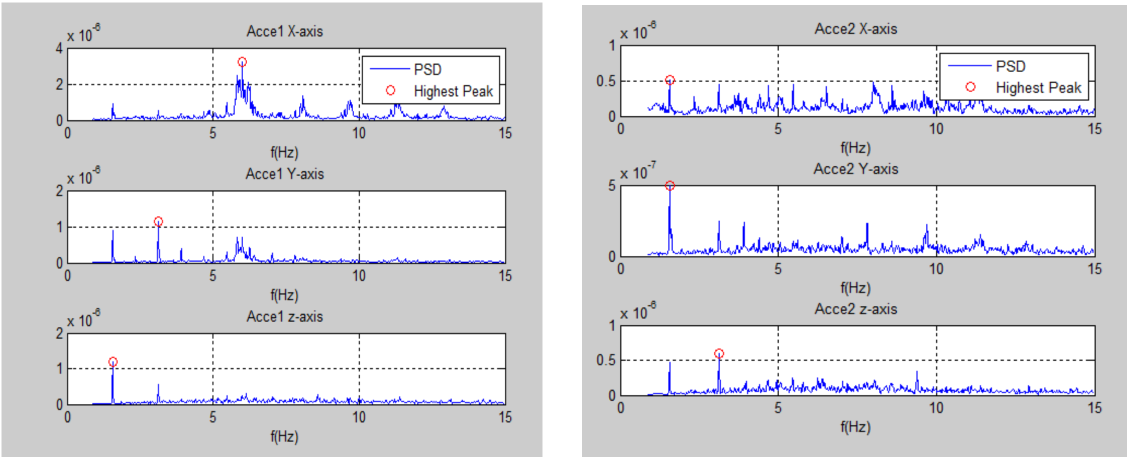


(a) (b)

Figure 3.8 RMS graphs of tremor signal for (a) right hand and (b) left hand

3.4.2.2 Highest Peak (HP)

Meaning of highest peak is the frequency of the highest peak in the assessed spectrum [27]. This feature was calculated in frequency domain. If highest peak values rise up when tremor signals of before exercise and after the exercise are compared, improving of tremor is expected. Highest peak graphs were drew by MATLAB that can given in Fig 3.9 (a) (b). Acce1 represent the sensor which was located on index finger of right hand and Acce2 represent the other sensor which was located on index finger of left hand.



(a) (b)

Figure 3.9 Highest peak value in (a) right hand tremor and (b) left hand tremor

3.4.2.3 Median Frequency (MDF)

The frequency below that exists 50% of the power in the spectrum and above which exists the other 50% [27]. Also this parameter was calculated in frequency domain as highest frequency. If median frequency values rise up when tremor signals of before exercise and after the exercise are compared, improving of tremor is expected. The mathematical expression for the median frequency can given in Equation (3.6).

$$MF(t) = \frac{\int_{0}^{f_s/2} f . S_{E_{t \to t+n}}(f)}{\int_{0}^{f_s/2} S_{E_{t \to t+n}}(f)} \qquad (3.6)$$

Where n lenght of window; S(f) the Power Spectral Density of tremor signal fragment E(t→t+n); f_s sampling frequency.

3.5 Statistical Analysis

To found out the variation in a quantitative data set statistically Measures of Variability have to calculate. The frequently used measures of variability is standard deviation (SD). It is simply a measurement of a sample's deviation from the mean of the distribution and its symbol is σ. SD can compute using Equation (3.7).

$$SD = \sqrt{\frac{\sum_{i=1}^{N}(x_i - \bar{x})^2}{n-1}} \qquad (3.7)$$

Each magnitude of the deviation in Eq. (3.7) is considered as sample's distance from the mean of the distribution. Using the SD value of two data set which have equal number of sample, less deviated dataset can find.

CHAPTER 4

RESULTS

Results were evaluated according to analysis of recorded signals.

4.1 Tremor Intensity (TI)

4.1.1 Tremor Intensity on the X Axial at A1 Position

Results showed that the TI on the x axial decreased on the second and eighth patients' right hands, and increased on the right hands of eight patients. Also it did not change on the right hands of third patient (Fig. 4.1). It decreased on the left hands of second patient, and increased on the left hands of seven patients and it did not differ for left hands of third and seventh subjects when results were compared on before wii and after wii (Fig. 4.2).

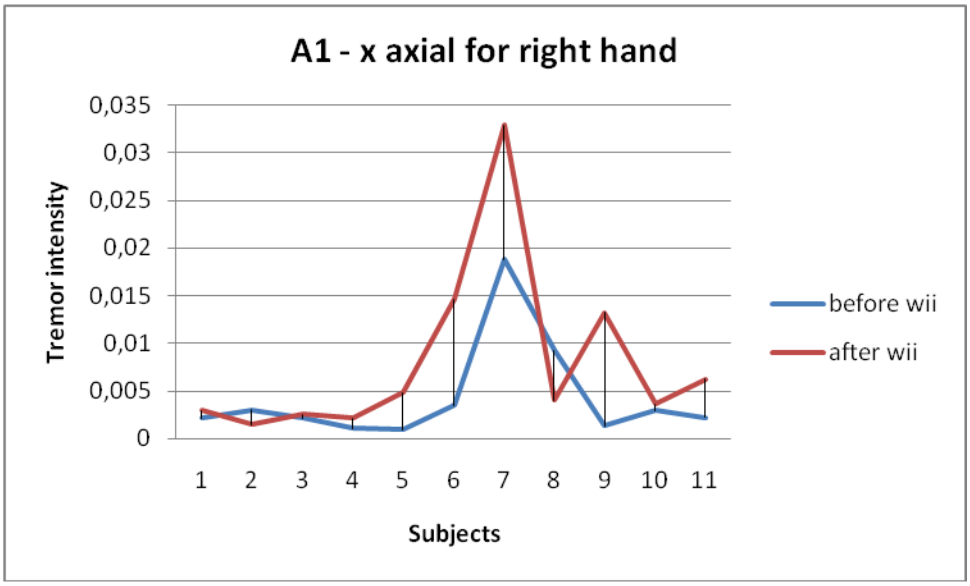


Figure 4.1 Differences in TI in x axial for right hand during A1 position

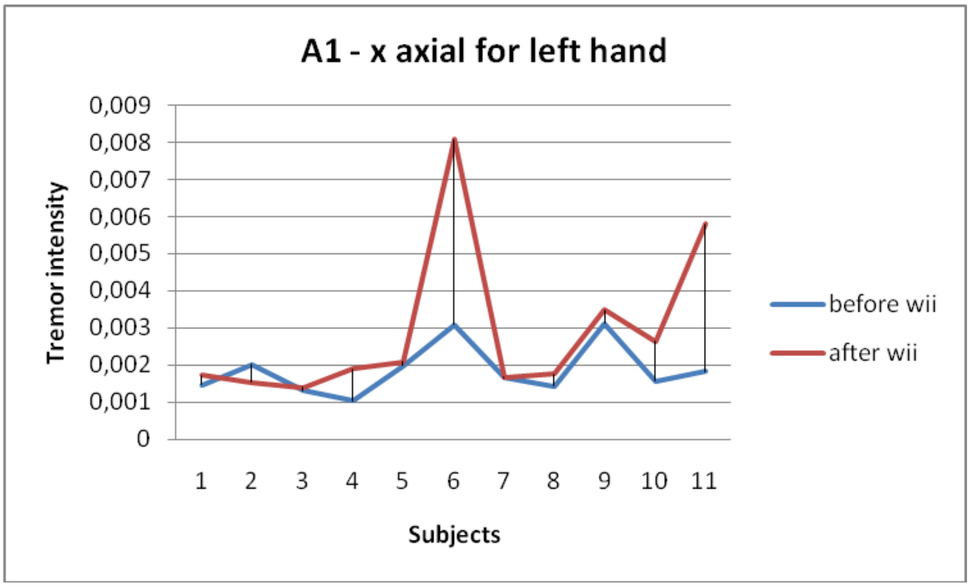


Figure 4.2 Differences in TI in x axial for left hand during A1 position

4.1.2 Tremor Intensity on the Y Axial at A1 Position

When the results were compared on before wii and after wii exercise, decreasing was seen on the right hands of second patient and no difference on the right hands of first and eighth patients, also increasing was seen on the other patients' right hands (Fig. 4.3). It decreased on only second patient's left hand. TI did not change on the left hands of first patient and it was stable for the other subjects' left hands (Fig. 4.4).

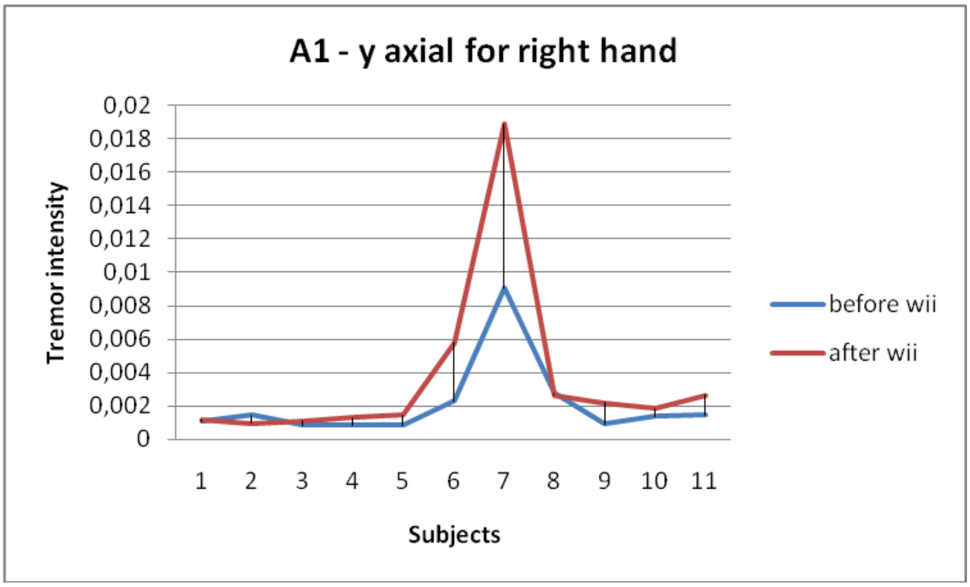


Figure 4.3 Differences in TI in y axial for right hand during A1 position

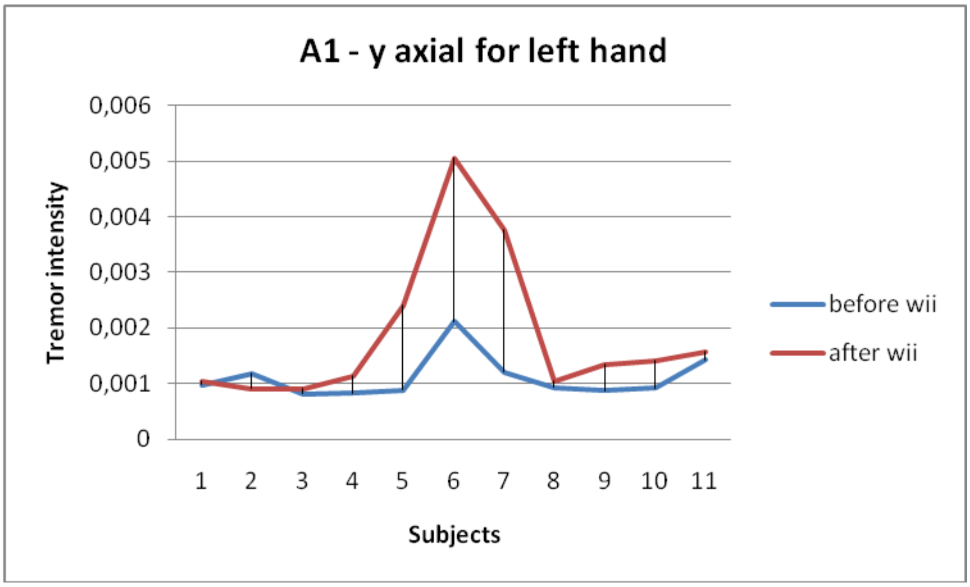


Figure 4.4 Differences in TI in y axial for left hand during A1 position

4.1.3 Tremor Intensity on the Z Axial at A1 Position

TI decreased on the right hands of second and eighth subjects, increased on the right hands of six patients and there is no difference on the right hands of first, third, and tenth patients at the end of wii exercise programme (Fig. 4.5). Also decreasing was seen on the left hands of second subject and increasing was seen on the left hands of the other subjects (Fig. 4.6).

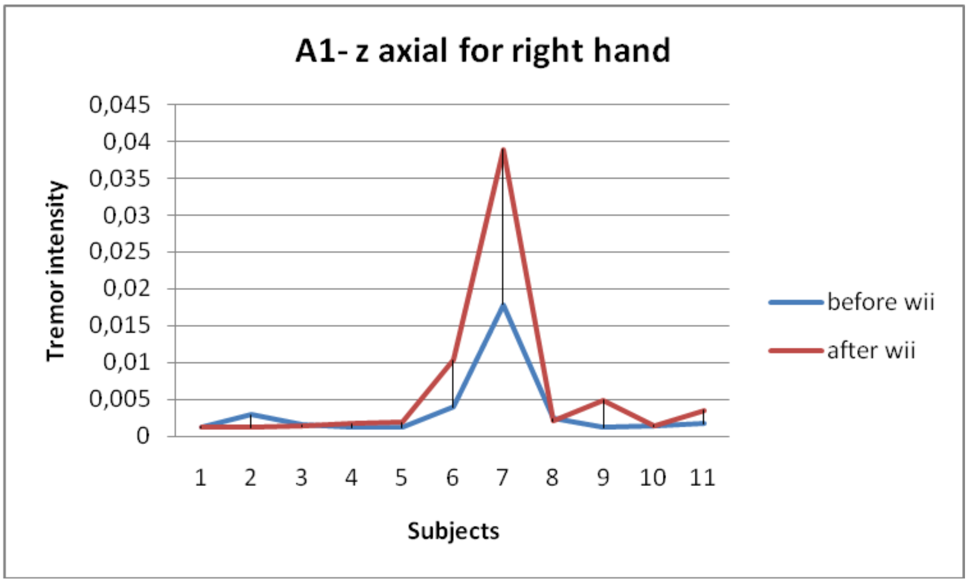


Figure 4.5 Differences in TI in z axial for right hand during A1 position

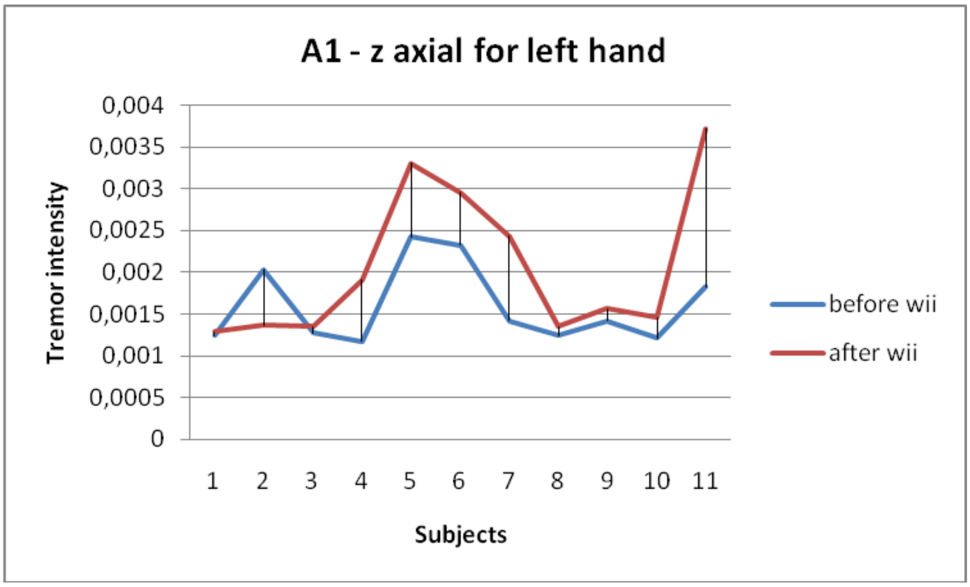


Figure 4.6 Differences in TI in z axial for left hand during A1 position

4.1.4 Tremor Intensity on the X Axial at A2 Position

TI decreased on the right hands of second and eighth subjects, increased on the rigth hands of third, sixth, and seventh patients and there is no difference on the right hands of the other subjects (Fig. 4.7). Also decreasing was seen on the left hands of first, second, seventh, and tenth subjects, did not change on the left hand of fifth patient, and increased on the left hands of the other subjects (Fig. 4.8).

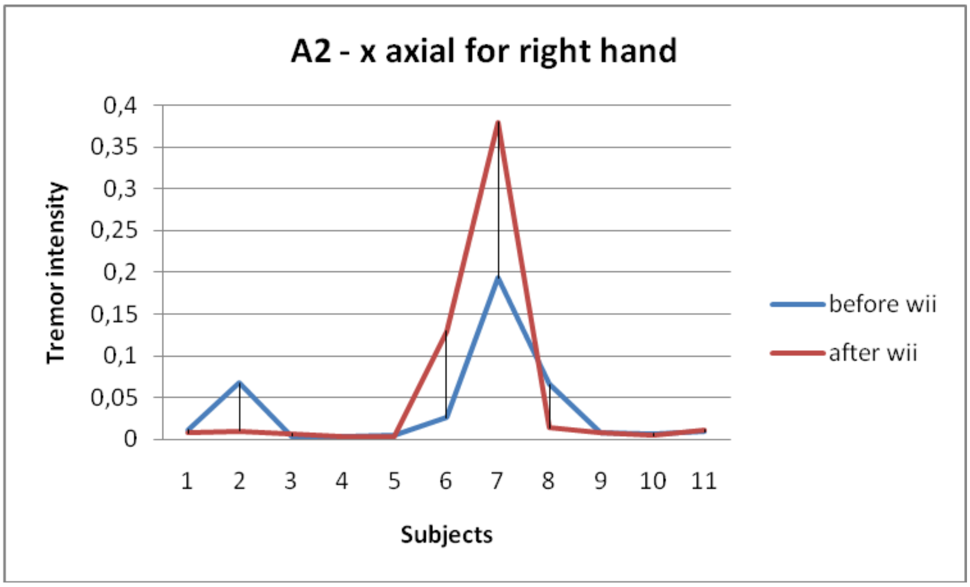


Figure 4.7 Differences in TI in x axial for right hand during A2 position

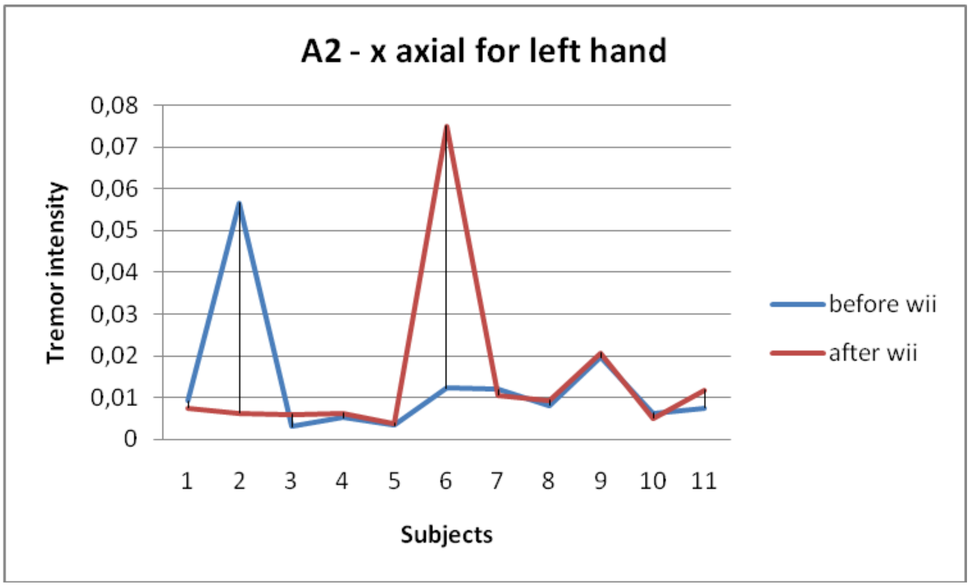


Figure 4.8 Differences in TI in x axial for left hand during A2 position

4.1.5 Tremor Intensity on the Y Axial at A2 Position

When the results were compared on before wii and after wii exercise, decreasing was seen on the right hands of second, eighth, and tenth patients, increasing was seen on the sixth and seventh patients, also no difference was seen on the right hands of other patients (Fig. 4.9). It did not change on only first patient's left hand. TI increased on the left hands of third, fourth, fifth, sixth, seventh, eighth, and eleventh patients and it was stable for the other subjects' left hands (Fig. 4.10).

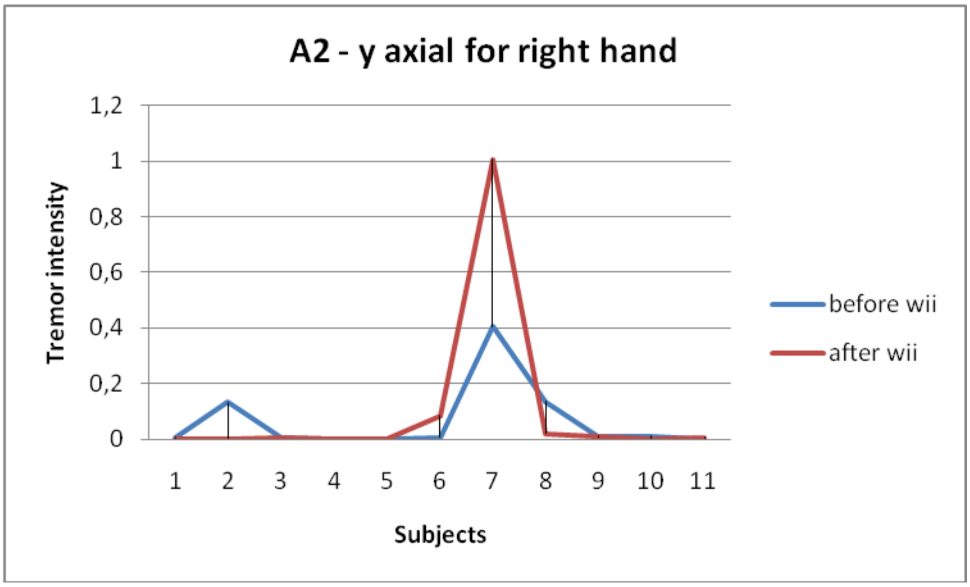


Figure 4.9 Differences in TI in y axial for right hand during A2 position

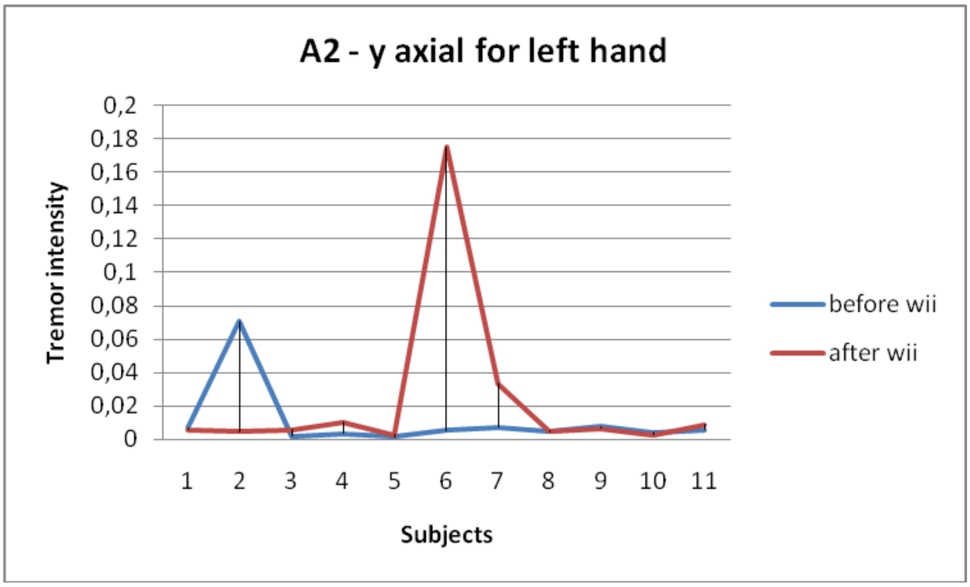


Figure 4.10 Differences in TI in y axial for left hand during A2 position

4.1.6 Tremor Intensity on the Z Axial at A2 Position

There was no difference on the right hands of first, fourth, and fifth patients, there was increasing on the right hands of sixth, seventh, and eleventh patients, also there was decreasing on the right hands of the other subjects at the end of the wii exercise programme (Fig. 4.11). For the left hands, no differences was observed on fifth patient, decreasing was observed on first, second, eighth, nineth, and tenth patients, also increasing was observed on the other patients at the end of the exercise programme (Fig. 4.12).

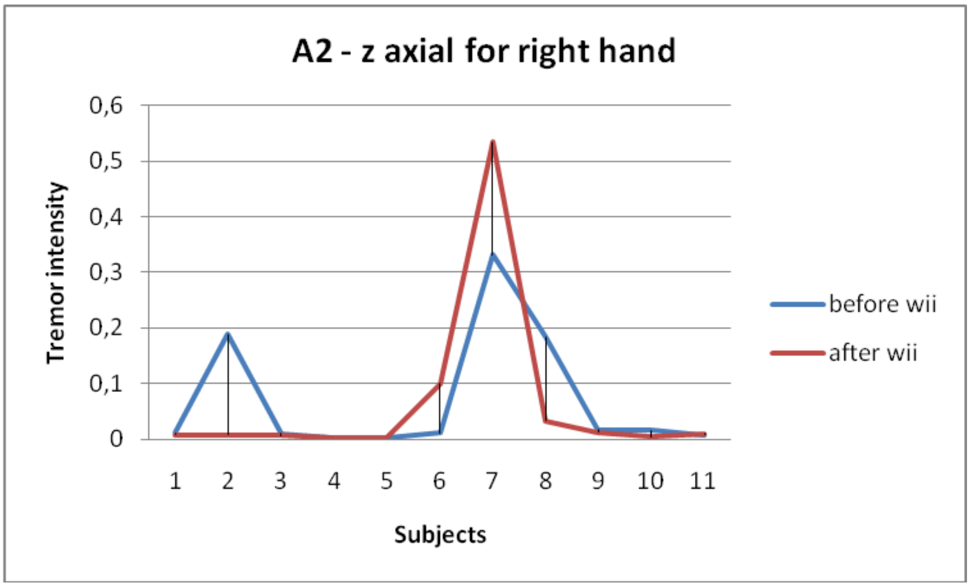


Figure 4.11 Differences in TI in z axial for right hand during A2 position

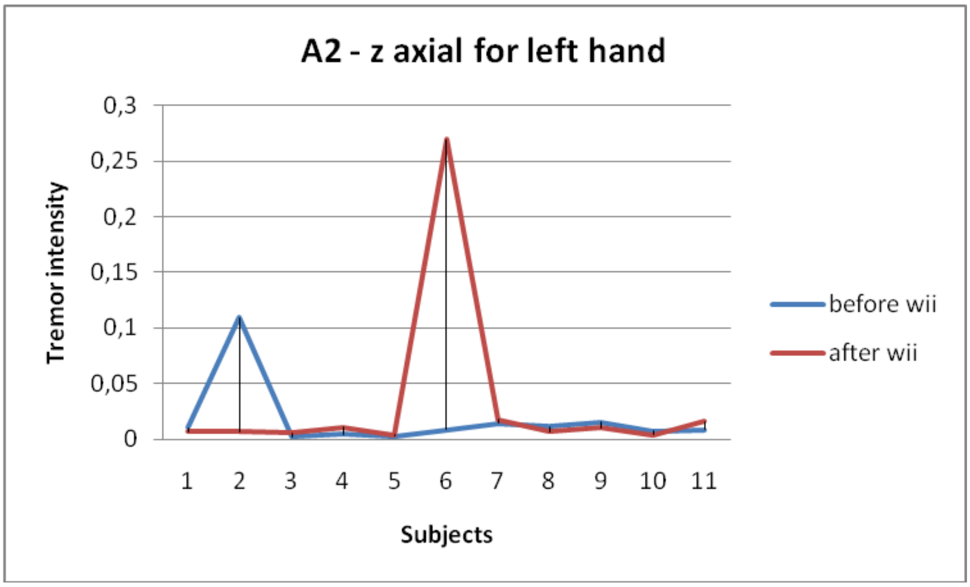


Figure 4.12 Differences in TI in z axial for left hand during A2 position

4.1.7 Tremor Intensity on the X Axial at A3 Position

TI decreased on the right hands of seventh, eighth, and tenth subjects, increased on the right hands of the other patients at the end of wii exercise programme (Fig. 4.13). Also decreasing was seen on the left hands of seventh, tenth, and eleventh subjects and increasing was seen on the left hands of the other subjects (Fig. 4.14).

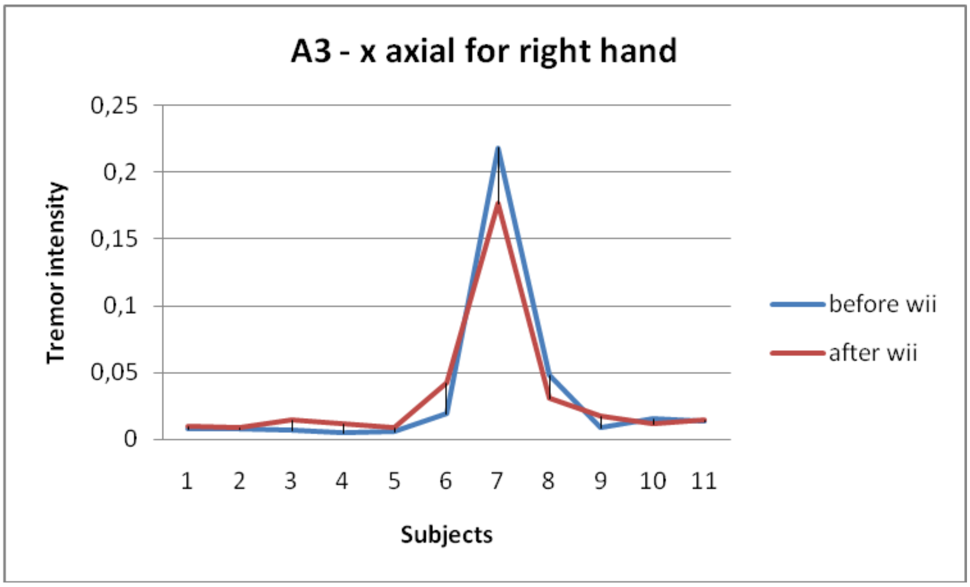


Figure 4.13 Differences in TI in x axial for right hand during A3 position

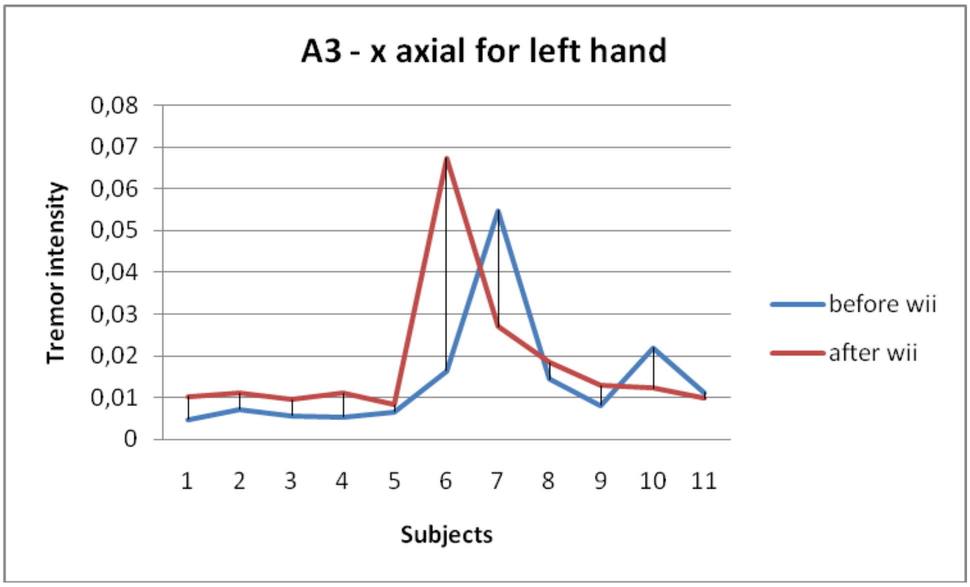


Figure 4.14 Differences in TI in x axial for left hand during A3 position

4.1.8 Tremor Intensity on the Y Axial at A3 Position

TI decreased on the right hands of seventh, tenth, and eleventh subjects, did not change on the right hands of first patient, and increased on the right hands of the other patients at the end of wii exercise programme (Fig. 4.15). Also decreasing was seen on the left hands of seventh, eighth, tenth, and eleventh subjects and increasing was seen on the left hands of the other subjects (Fig. 4.16).

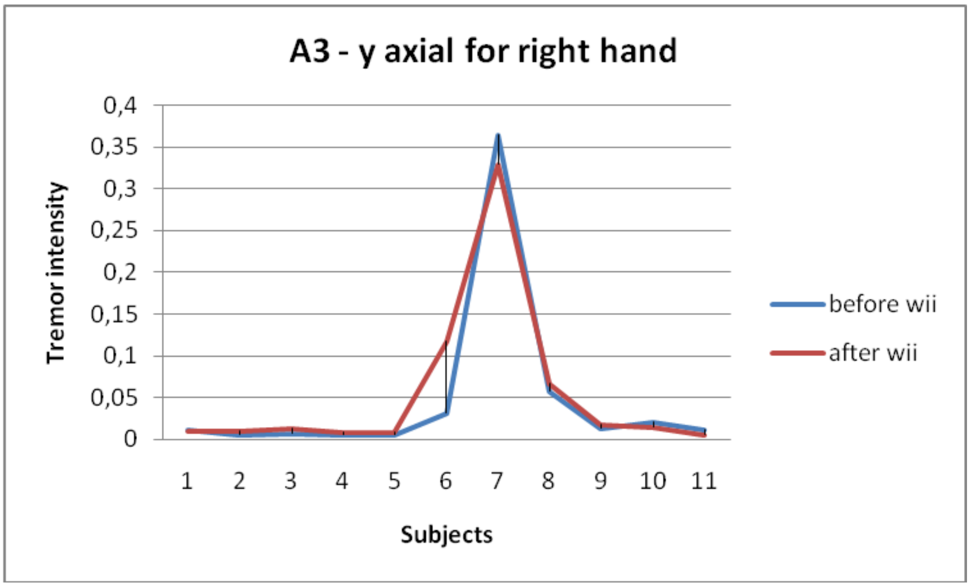


Figure 4.15 Differences in TI in y axial for right hand during A3 position

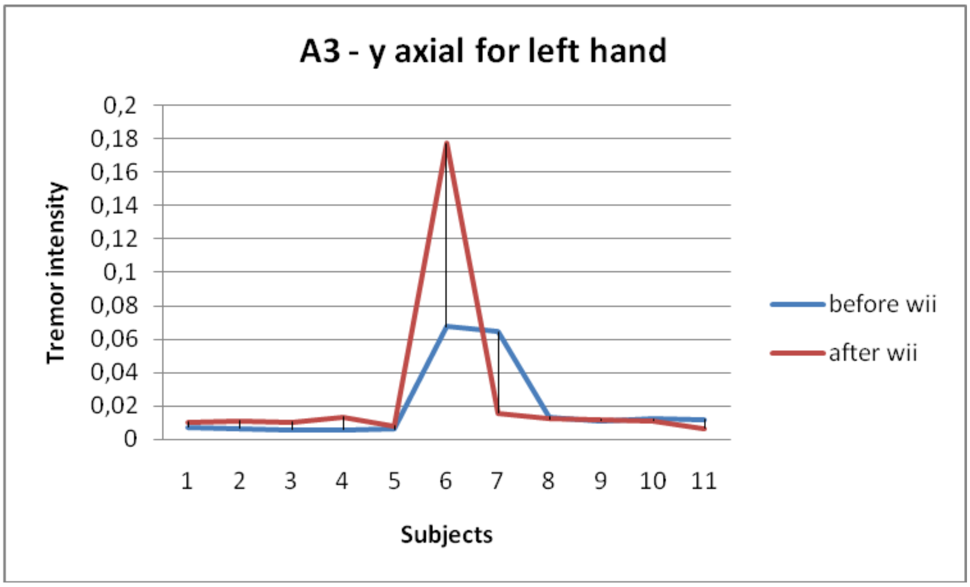


Figure 4.16 Differences in TI in y axial for left hand during A3 position

4.1.9 Tremor Intensity on the Z Axial at A3 Position

There was no difference on the right hand of fifth patient, there was increasing on the right hands of second, third, and fourth, seventh, nineth, and eleventh patients, also there was decreasing on the right hands of the other subjects at the end of the wii exercise programme (Fig. 4.17). For the left hands, decreasing was observed on seventh, eighth, and tenth patients, also increasing was observed on the other patients at the end of the exercise programme (Fig. 4.18).

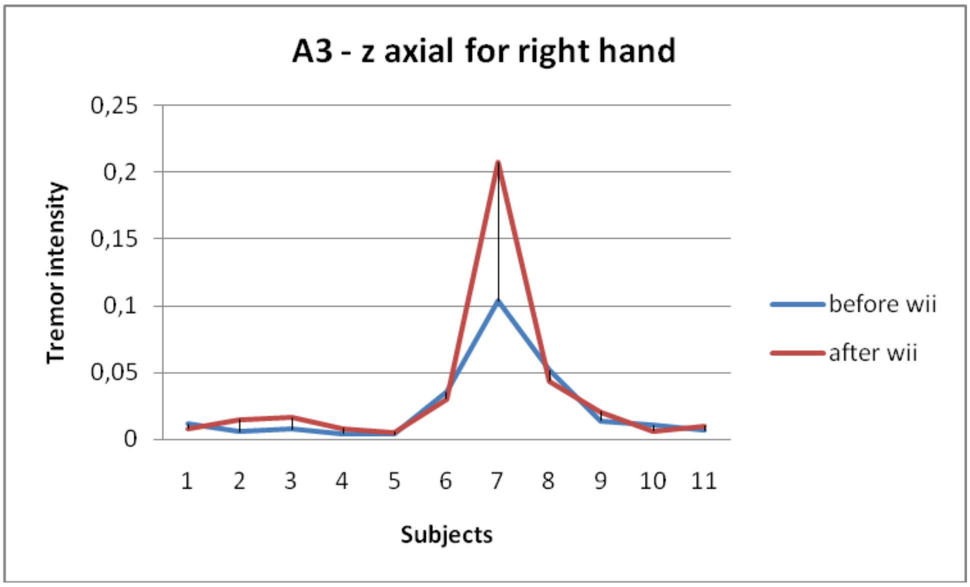


Figure 4.17 Differences in TI in z axial for right hand during A3 position

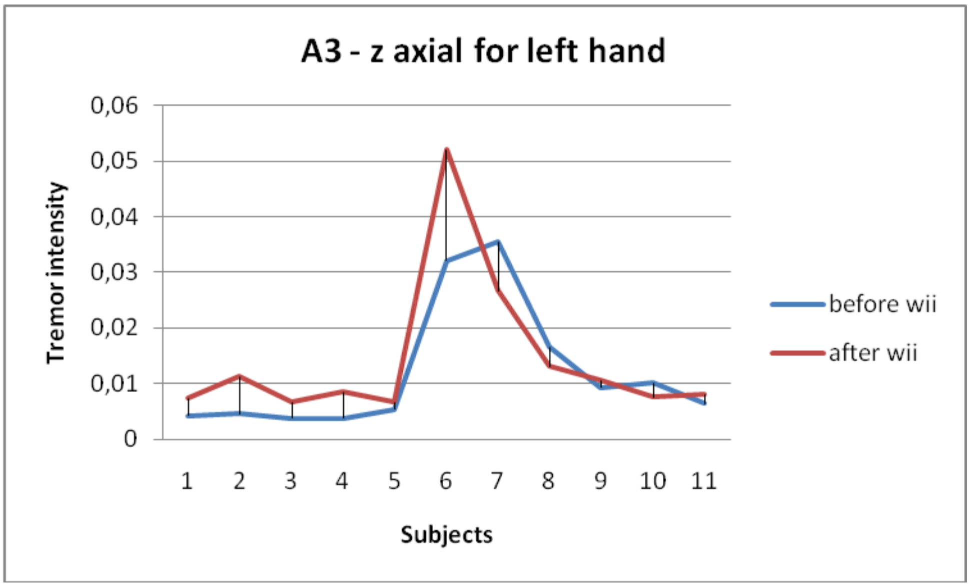


Figure 4.18 Differences in TI in z axial for left hand during A3 position

When mean variables were evaluated, seen that the TI increased after wii exercise programme. Although, there were no significant differences between before and after wii exercise on some patients' TI, increasing was observed at the end of the study (Table 4.1).

Table 4.1 Mean and Standard deviation variables of tremor intensity before wii exercise and after wii exercise

Recording case	Axial and hand	Mean and Standard deviation	
		Before exerxise	After exercise
A1	X axial right hand	0,00429±0,0545	0,00802±0,0093
	X axial left hand	0,00206±0,0024	0,00364±0,0052
	Y axial right hand	0,00331±0,0049	0,00623±0,0112
	Y axial left hand	0,00187±0,0007	0,00291±0,0021
	Z axial right hand	0,00110±0,0004	0,00187±0,0014
	Z axial left hand	0,00160±0,0005	0,00206±0,0009
A2	X axial right hand	0,03631±0,0573	0,05265±0,1147
	X axial left hand	0,06647±0,1237	0,10497±0,2998
	Y axial right hand	0,07132±0,1113	0,06589±0,1578
	Y axial left hand	0,01298±0,0152	0,01418±0,0205
	Z axial right hand	0,01075±0,0199	0,02364±0,0509
	Z axial left hand	0,01765±0,0306	0,03257±0,0786
A3	X axial right hand	0,03212±0,0629	0,03214±0,0492
	X axial left hand	0,04865±0,1058	0,05462±0,0972
	Y axial right hand	0,02300±0,0306	0,03377±0,0586
	Y axial left hand	0,01426±0,0145	0,01793±0,0172
	Z axial right hand	0,01932±0,0232	0,02622±0,0501
	Z axial left hand	0,01198±0,0114	0,01436±0,0137

4.2 Highest Peak (HP)

4.2.1 Highest Peak on the X Axial at A1 Position

When the results were compared on before wii and after wii exercise, increasing was seen on the right hand of first patient and decreasing was seen on the right hands of other patients (Fig. 4.19). HP increased on the left hands of first patient and dicreased on the other subjects’ left hands (Fig. 4.20).

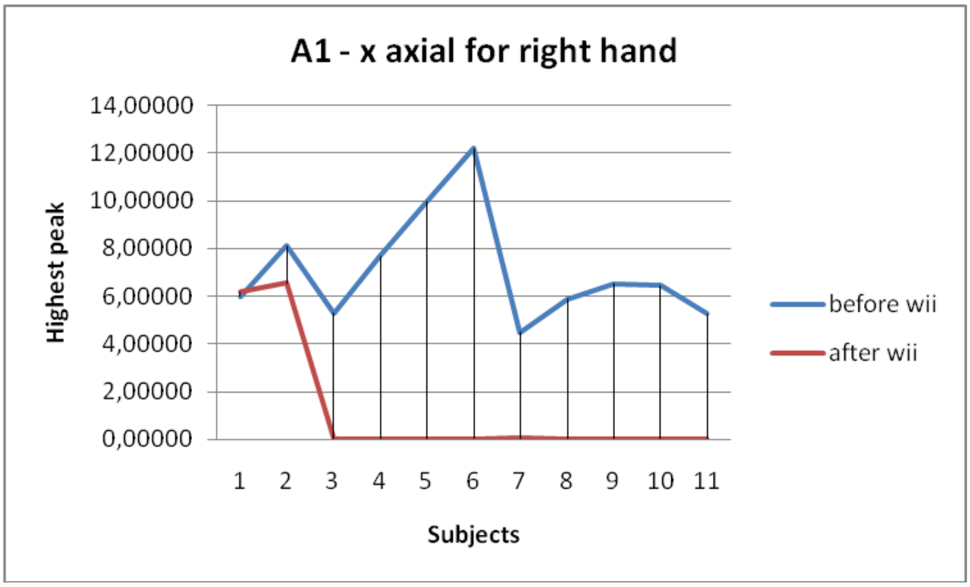


Figure 4.19 Differences in HP in x axial for right hand during A1 position

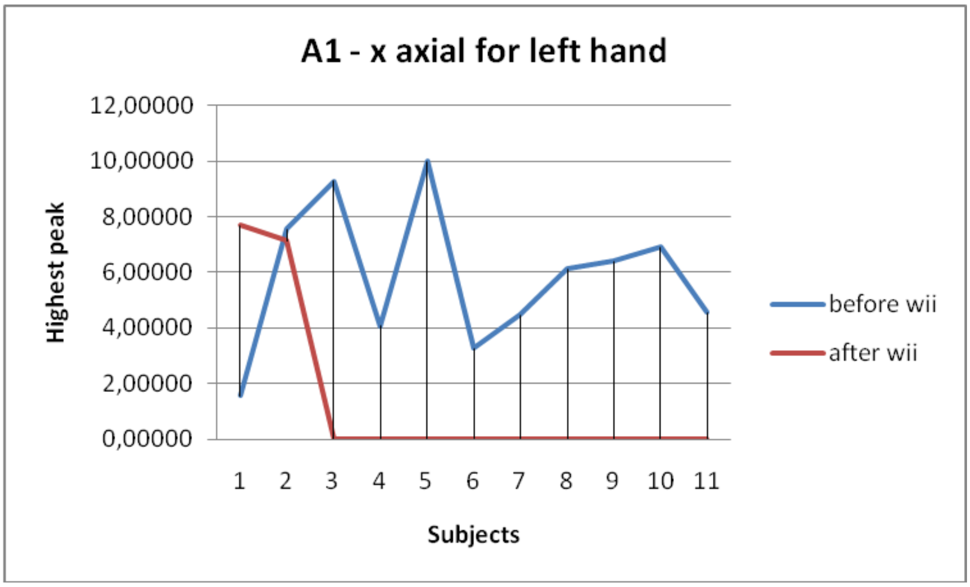


Figure 4.20 Differences in HP in x axial for left hand during A1 position

4.2.2 Highest Peak on the Y Axial at A1 Position

HP increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.21). Also it increased on the left hands of first and second patients, decreased on the left hands of the other patients (Fig. 4.22).

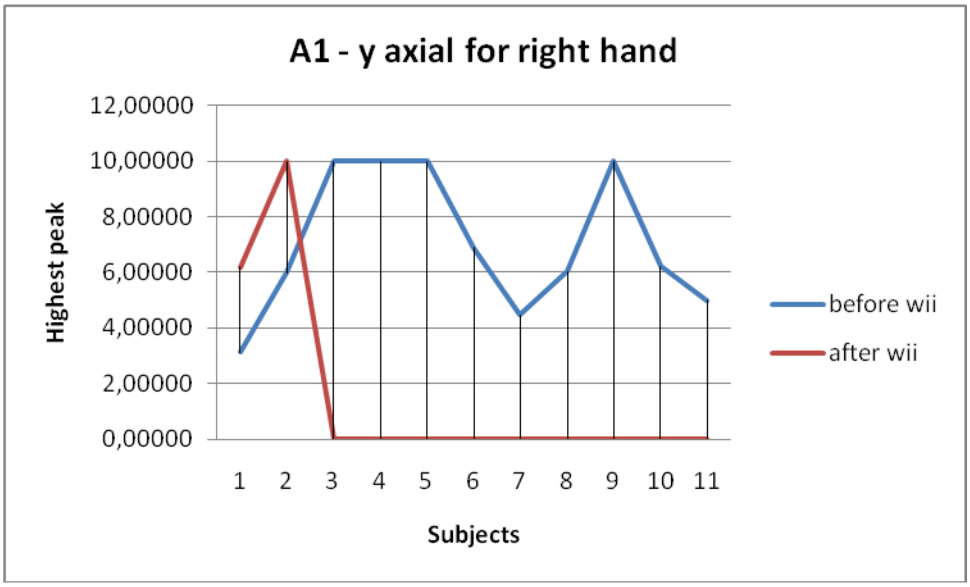


Figure 4.21 Differences in HP in y axial for right hand during A1 position

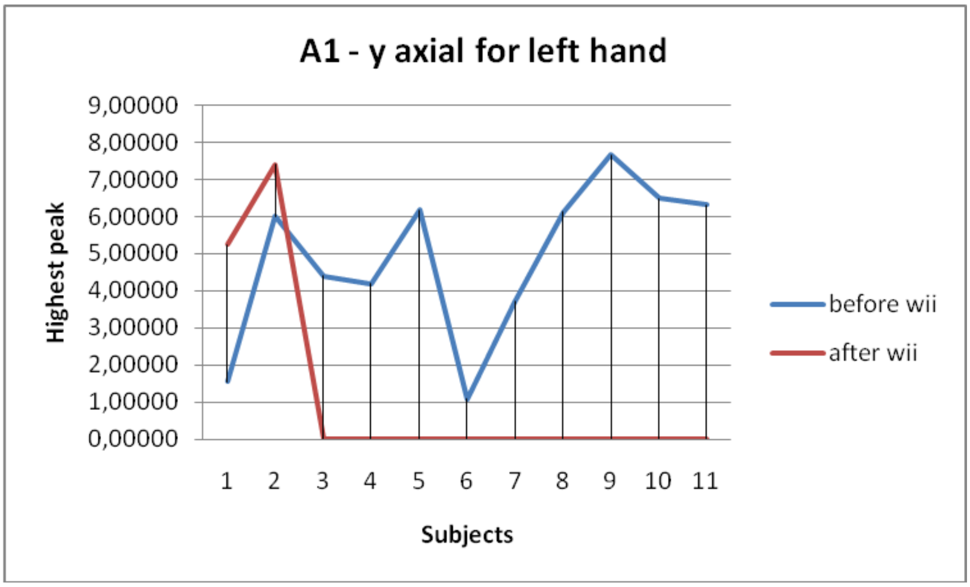


Figure 4.22 Differences in HP in y axial for left hand during A1 position

4.2.3 Highest Peak on the Z Axial at A1 Position

HP increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.23). Also it increased on the left hands of first and second patients, decreased on the left hands of the other patients (Fig. 4.24).

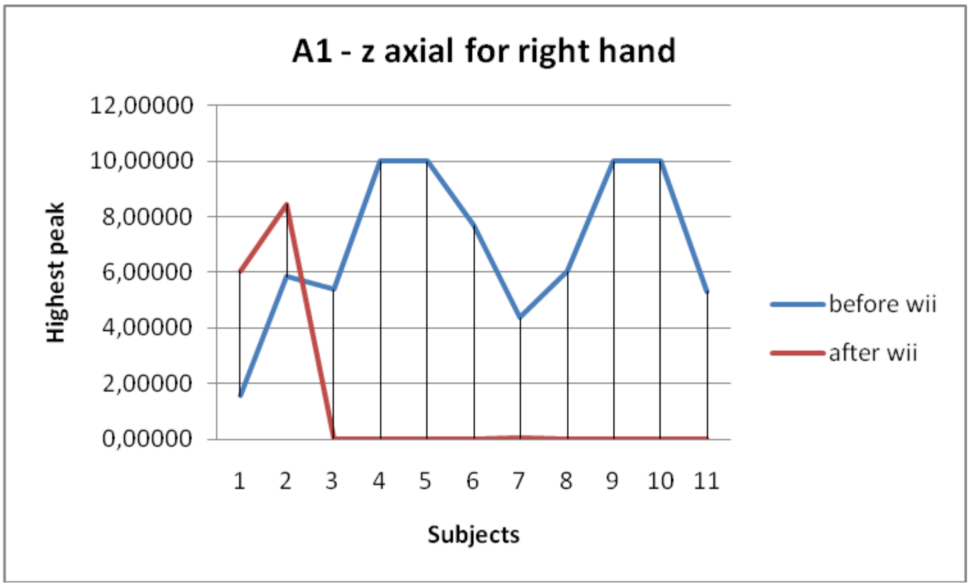


Figure 4.23 Differences in HP in z axial for right hand during A1 position

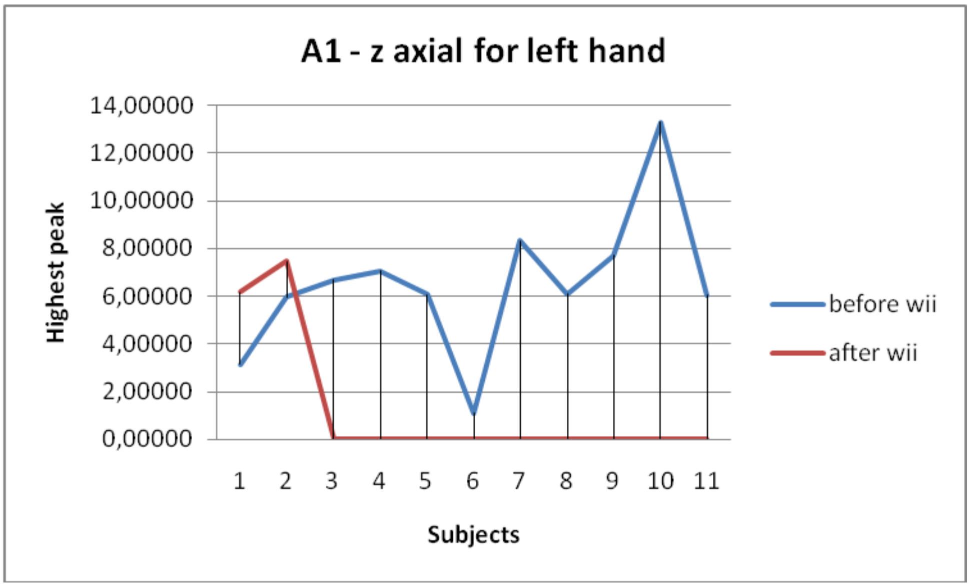


Figure 4.24 Differences in HP in z axial for left hand during A1 position

4.2.4 Highest Peak on the X Axial at A2 Position

HP increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.25). Also it increased on the left hands of first and second patients, decreased on the left hands of the other patients (Fig. 4.26).

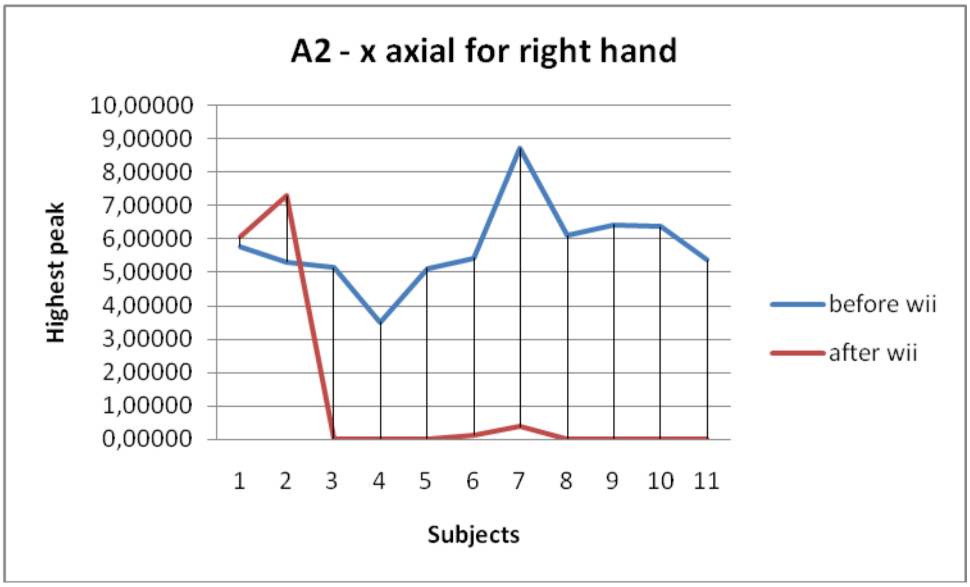


Figure 4.25 Differences in HP in x axial for right hand during A2 position

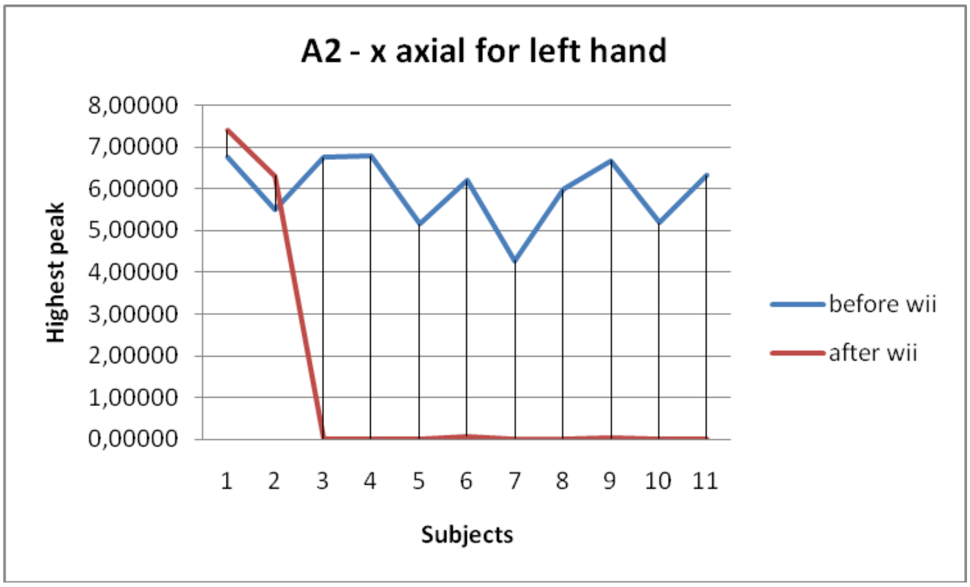


Figure 4.26 Differences in HP in x axial for left hand during A2 position

4.2.5 Highest Peak on the Y Axial at A2 Position

There were increasing on the right hands of first and second patients, decreasing on the right hands of the other patients (Fig. 4.27). Also, there was increasing on the left hand of seco88nd patient and decreasing on the left hands of the other patients (Fig. 4.28).

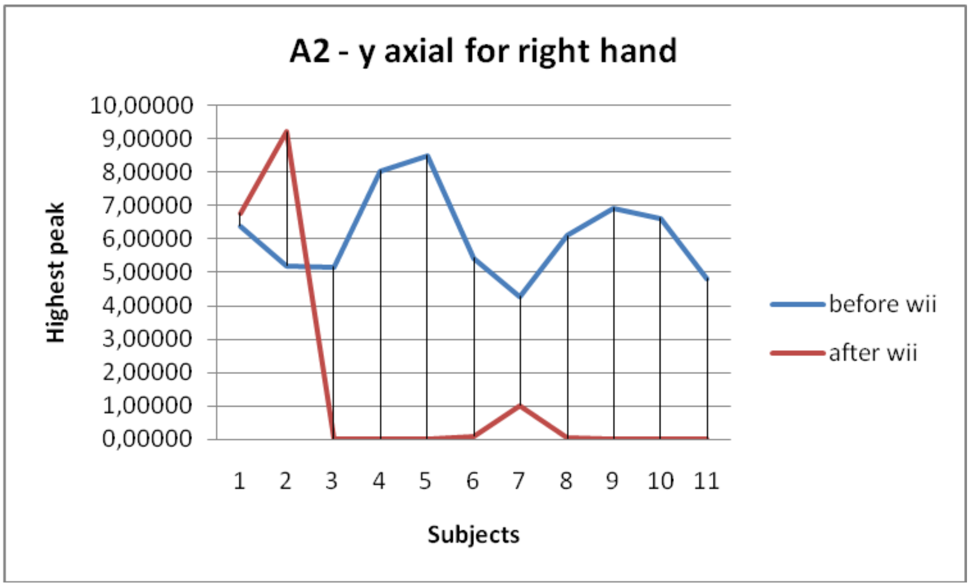


Figure 4.27 Differences in HP in y axial for right hand during A2 position

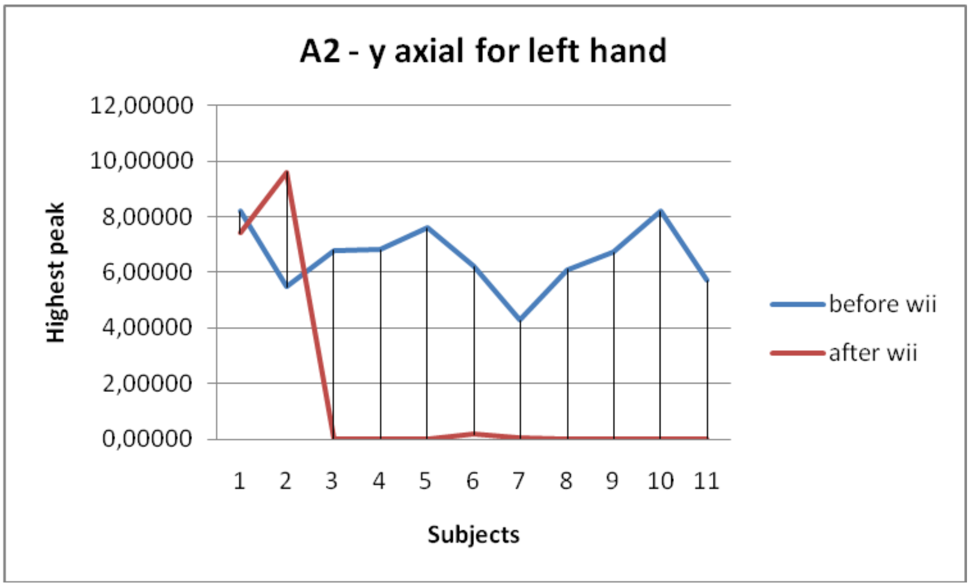


Figure 4.28 Differences in HP in y axial for left hand during A2 position

4.2.6 Highest Peak on the Z Axial at A2 Position

When the results were compared at the end of the exercise programme, increasing was seen on the right hand of second subject and decrasing was seen on the right hands of the other subjects (Fig. 4.29). Also, increasing was seen on the left hands of first and second patients, decreasing was seen on the other patients’ left hands (Fig. 4.30).

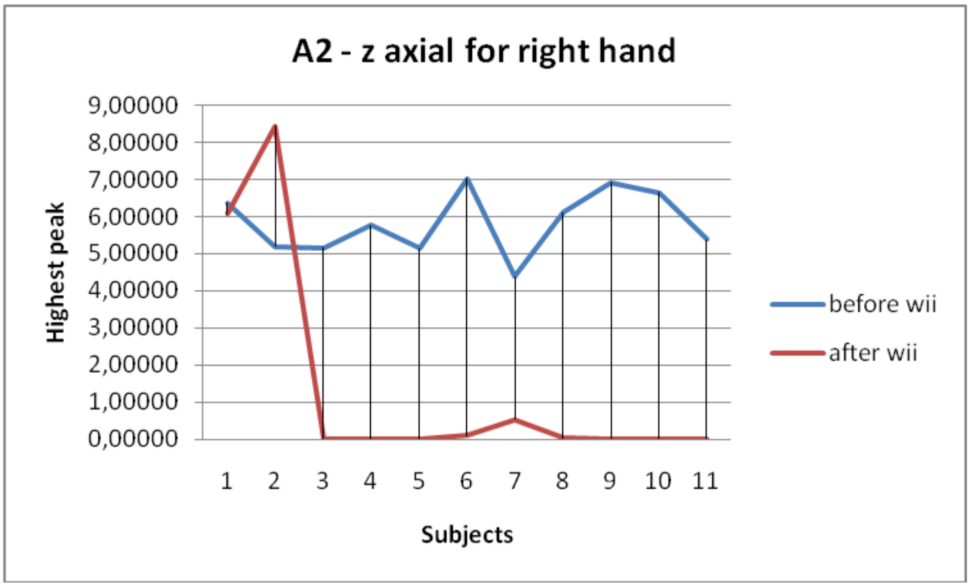


Figure 4.29 Differences in HP in z axial for right hand during A2 position

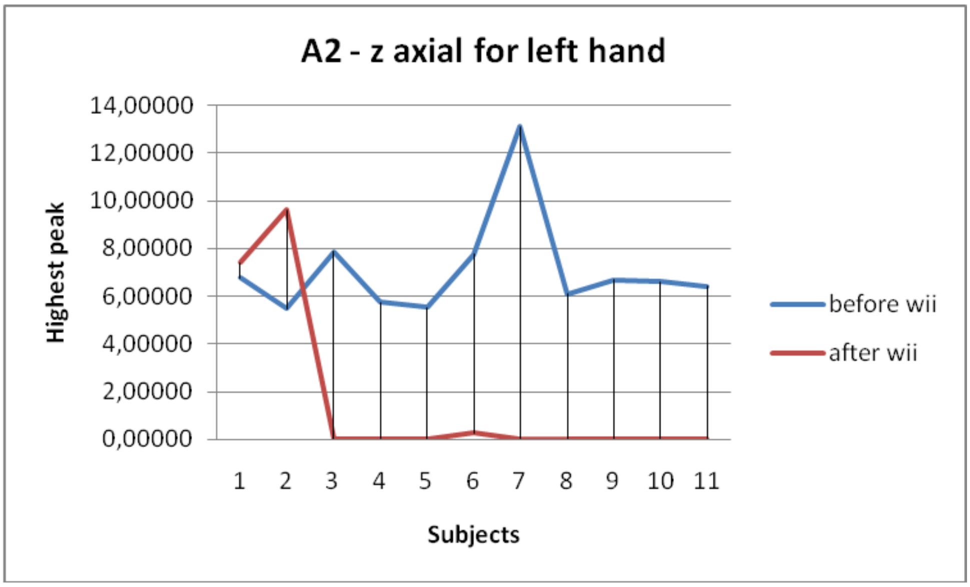


Figure 4.30 Differences in HP in z axial for left hand during A2 position

4.2.7 Highest Peak on the X Axial at A3 Position

HP increased on the right hand of second patient and decreased on the right hands of the other patients (Fig. 4.31). Also it increased on the left hand of second patient and decreased on the left hands of the other patients (Fig. 4.32).

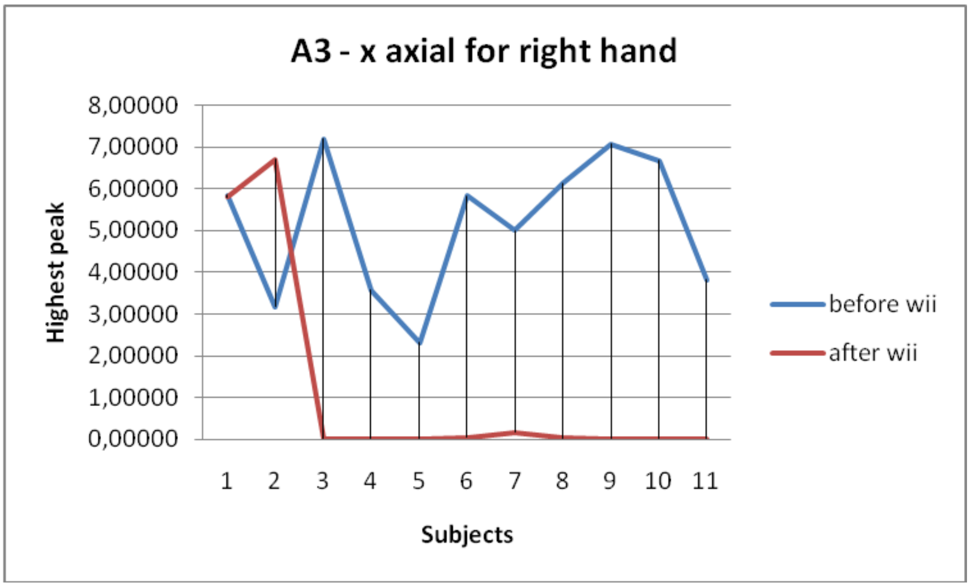


Figure 4.31 Differences in HP in x axial for right hand during A3 position

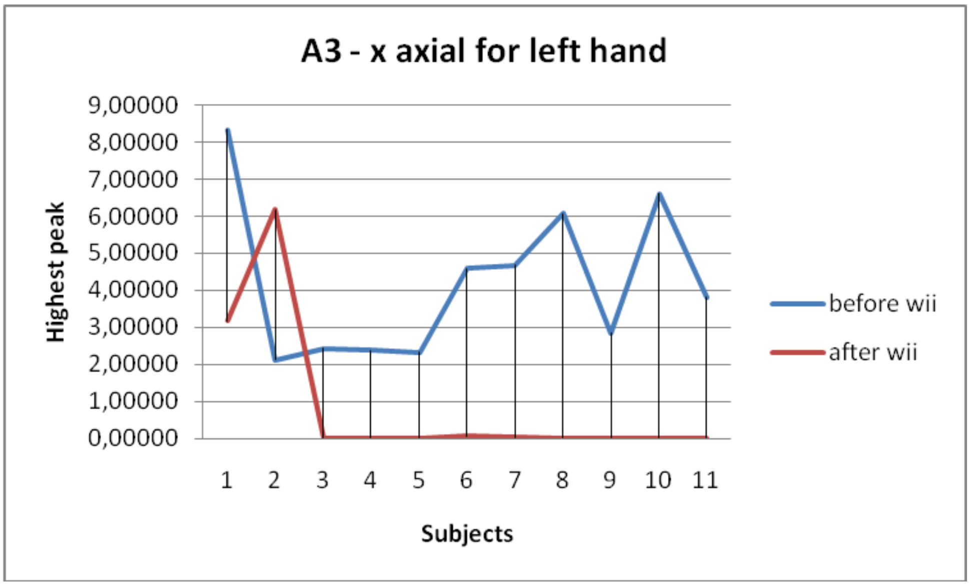


Figure 4.32 Differences in HP in x axial for left hand during A3 position

4.2.8 Highest Peak on the Y Axial at A3 Position

HP increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.33). Also it increased on the left hand of second patient and decreased on the left hands of the other patients (Fig. 4.34).

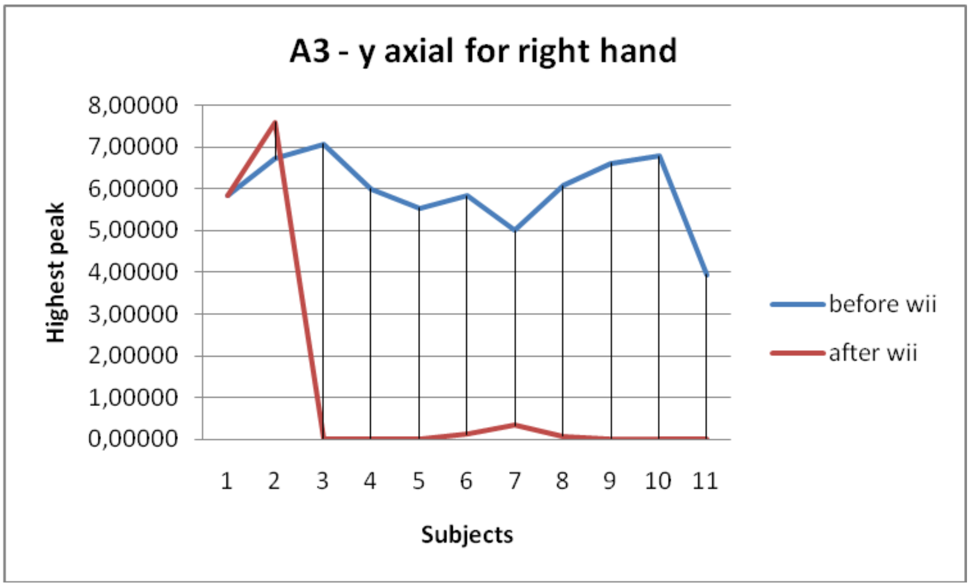


Figure 4.33 Differences in HP in y axial for right hand during A3 position

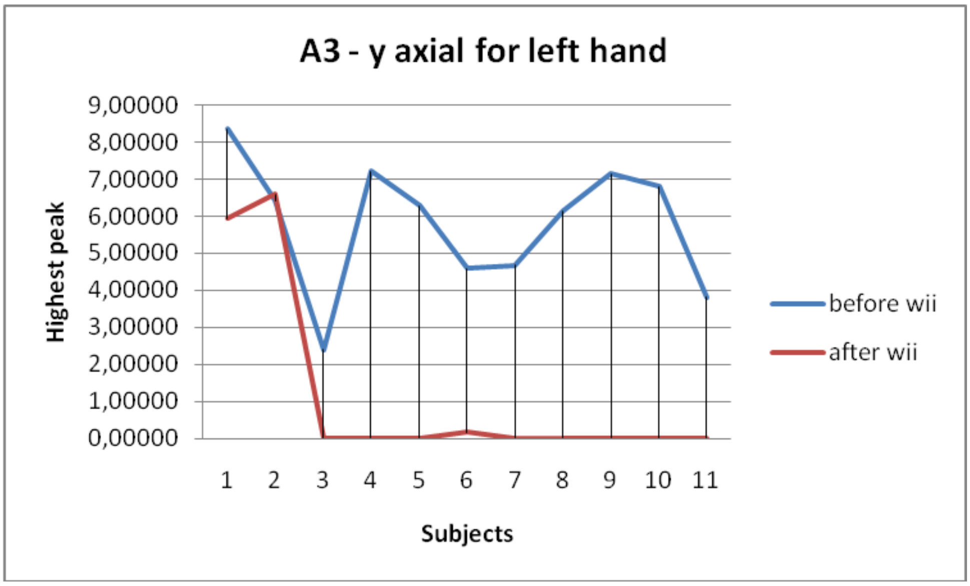


Figure 4.34 Differences in HP in y axial for left hand during A3 position

4.2.9 Highest Peak on the Z Axial at A3 Position

HP increased on the right hand of second patient and decreased on the right hands of the other patients (Fig. 4.35). Also it increased on the left hands of first and second patients, decreased on the left hands of the other patients (Fig. 4.36).

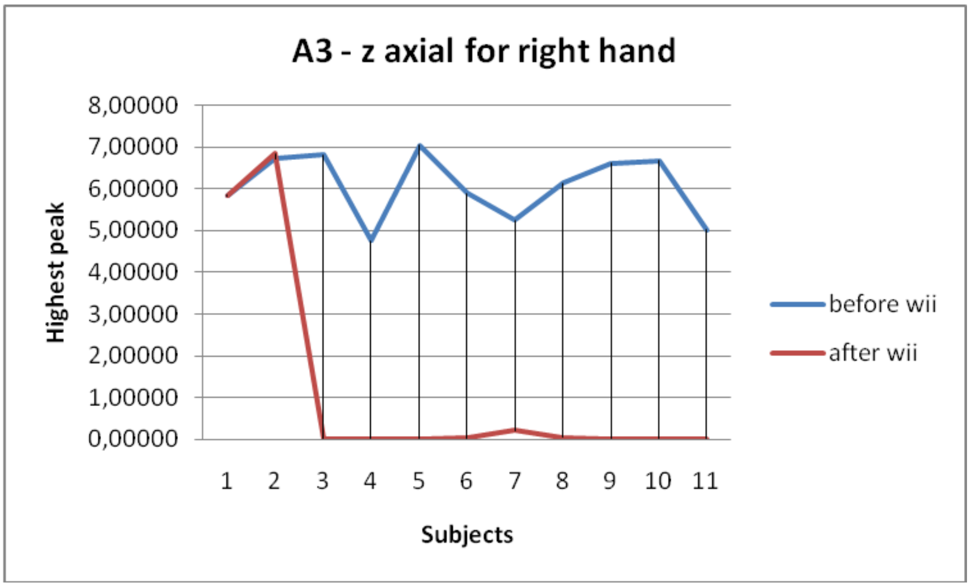


Figure 4.35 Differences in HP in z axial for right hand during A3 position

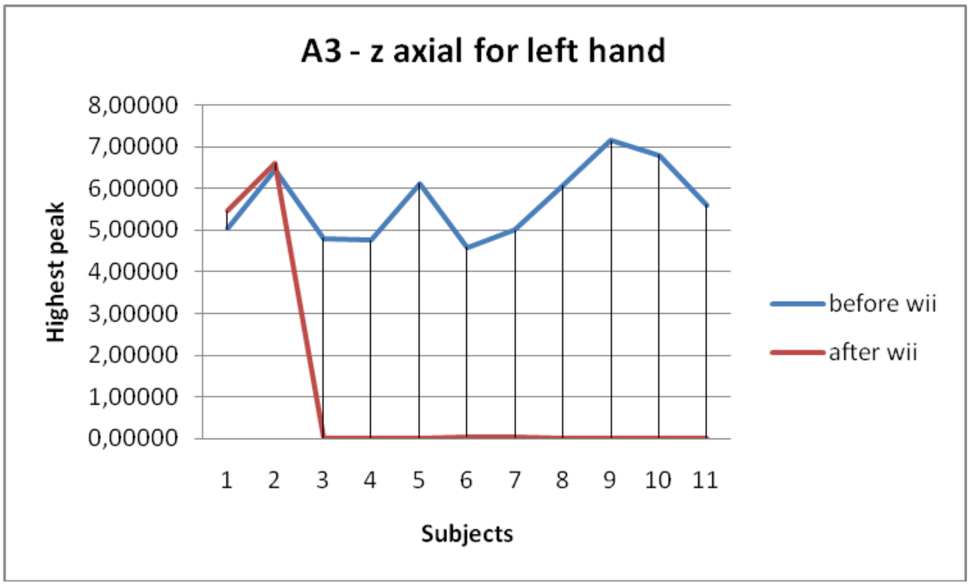


Figure 4.36 Differences in HP in z axial for left hand during A3 position

When mean variables were evaluated, seen that the HP decreased without Z axial for right hand at A2 position after wii exercise programme. There were significant differences between the HP values of before wii exercise and after wii exercise at the end of the study (Table 4.2).

Table 4.2 Mean and Standard deviation variables of highest peak before wii exercise and after wii exercise

Recording case	Axial and hand	Mean and Standard deviation	
		Before exerxise	After exercise
A1	X axial right hand	7,07453±2,2907	1,16470±2,5714
	X axial left hand	7,05788±2,5287	1,47406±3,3790
	Y axial right hand	6,91917±2,8385	1,32523±2,9806
	Y axial left hand	5,82747±2,5519	1,34964±2,9981
	Z axial right hand	4,88004±2,1055	1,15171±2,6025
	Z axial left hand	6,49470±3,0392	1,23920±2,7676
A2	X axial right hand	5,75256±1,2624	1,26202±2,6857
	X axial left hand	6,12848±1,3293	1,55506±3,2368
	Y axial right hand	5,82200±0,8541	1,38364±2,9550
	Y axial left hand	5,95509±0,8300	1,25923±2,7757
	Z axial right hand	6,54047±1,1760	11,56941±3,4648
	Z axial left hand	7,09118±2,1409	1,57940±3,4646
A3	X axial right hand	5,14915±1,6775	1,16567±2,5215
	X axial left hand	5,94399±0,8998	1,27630±2,7255
	Y axial right hand	6,06606±0,7816	1,18162±2,5537
	Y axial left hand	4,20310±2,0733	0,86633±2,0003
	Z axial right hand	5,80111±1,7400	1,16315±2,5265
	Z axial left hand	5,66933±0,8920	1,10715±2,4423

4.3 Median Frequency (MDF)

4.3.1 Median Frequency on the X Axial at A1 Position

MDF increased on the right hand of first patient and decreased on the right hands of the other patients (Fig. 4.37). Also it decreased on the left hands of all of the patients (Fig. 4.38).

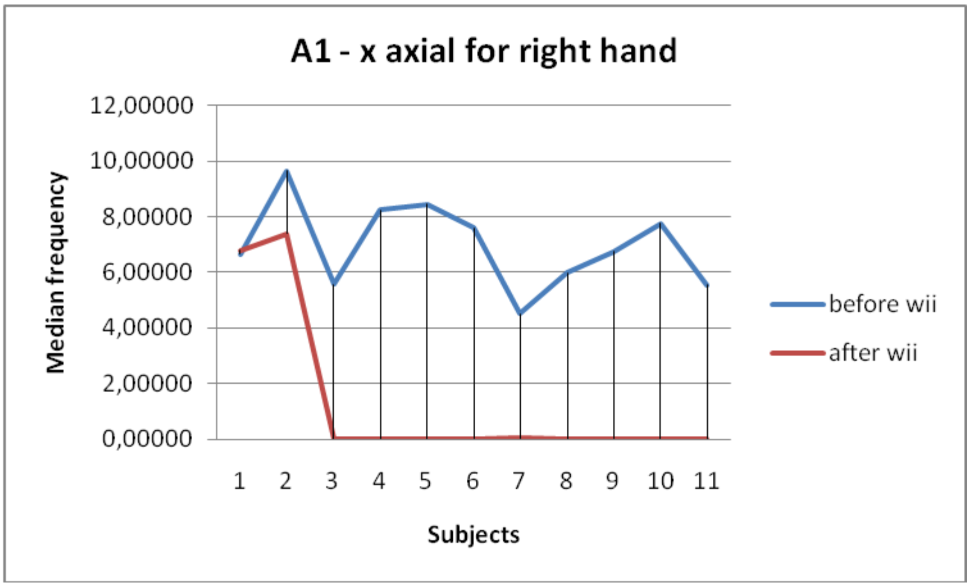


Figure 4.37 Differences in MDF in x axial for right hand during A1 position

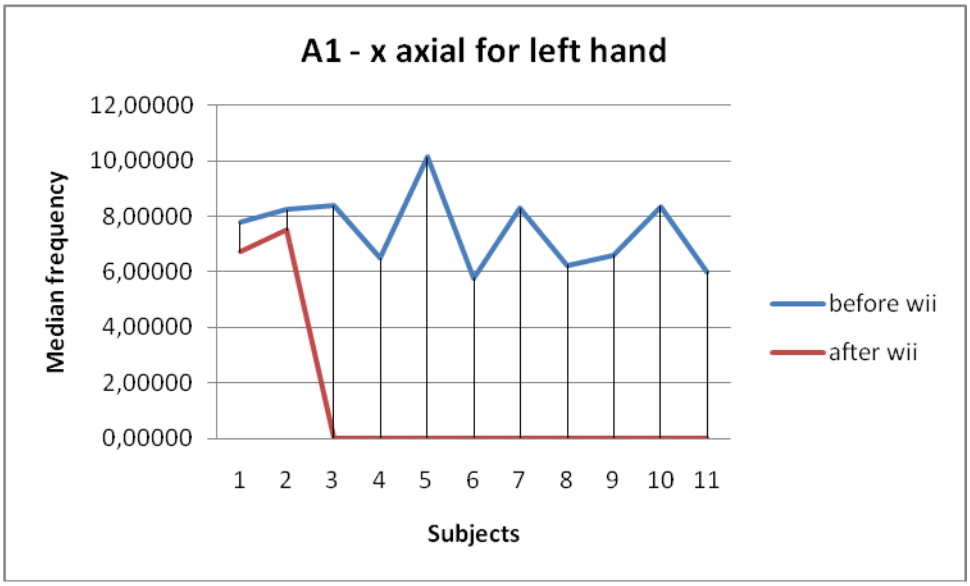


Figure 4.38 Differences in MDF in x axial for left hand during A1 position

4.3.2 Median Frequency on the Y Axial at A1 Position

MDF increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.39). Also it increased on the left hand of second patient and decreased on the left hands of the other patients (Fig. 4.40).

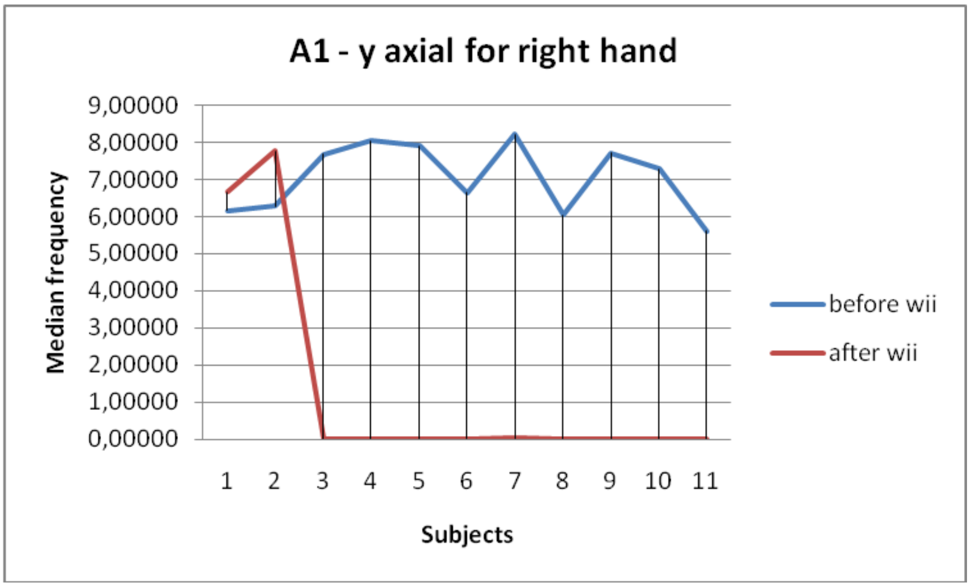


Figure 4.39 Differences in MDF in y axial for right hand during A1 position

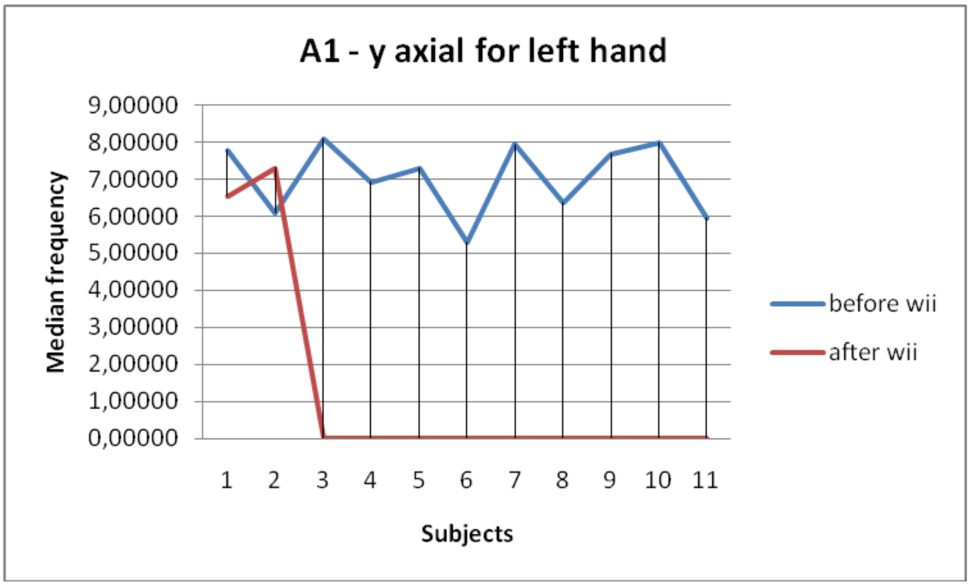


Figure 4.40 Differences in MDF in y axial for left hand during A1 position

4.3.3 Median Frequency on the Z Axial at A1 Position

MDF increased on the right hands of first and second patients, decreased on the right hands of the other patients (Fig. 4.41). Also it increased on the left hands of first and second patients, decreased on the left hands of the other patients (Fig. 4.42).

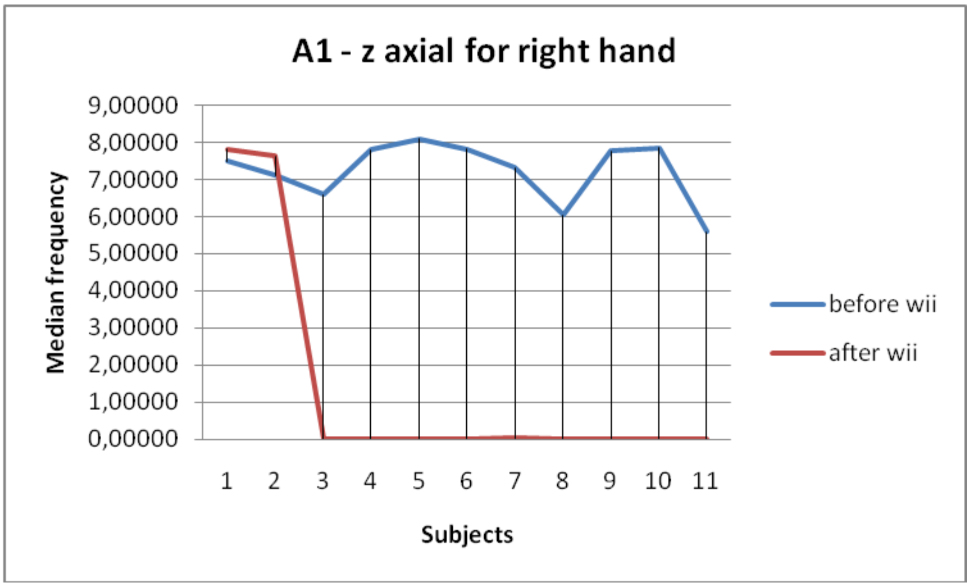


Figure 4.41 Differences in MDF in z axial for right hand during A1 position

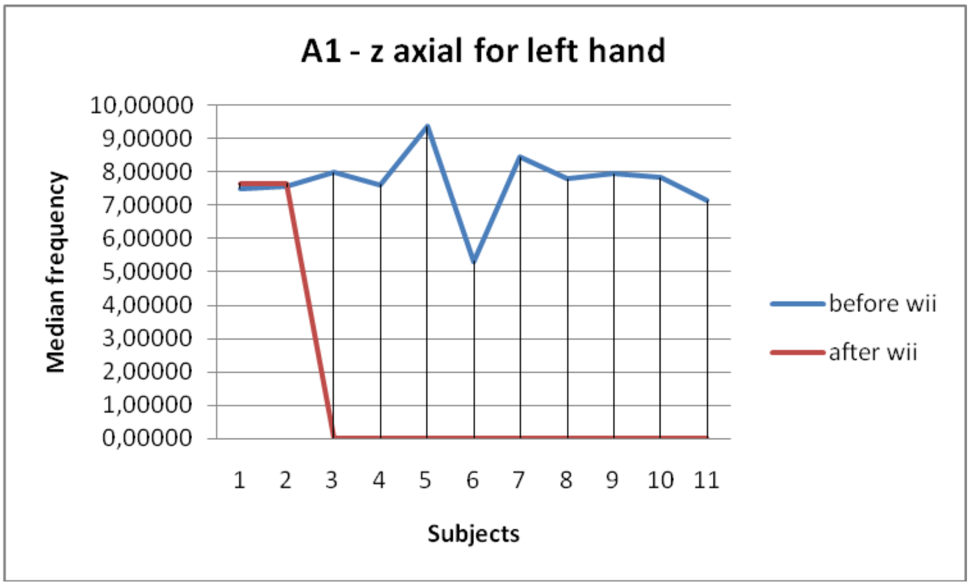


Figure 4.42 Differences in MDF in z axial for left hand during A1 position

4.3.4 Median Frequency on the X Axial at A2 Position

When the results were compared at the end of the exercise programme increasing was seen on the right hand of first subject and decrasing was seen on the right hands of the other subjects (Fig. 4.43). Also, increasing was seen on the left hands of first and second patients, decreasing was seen on the other patients' left hands (Fig. 4.44).

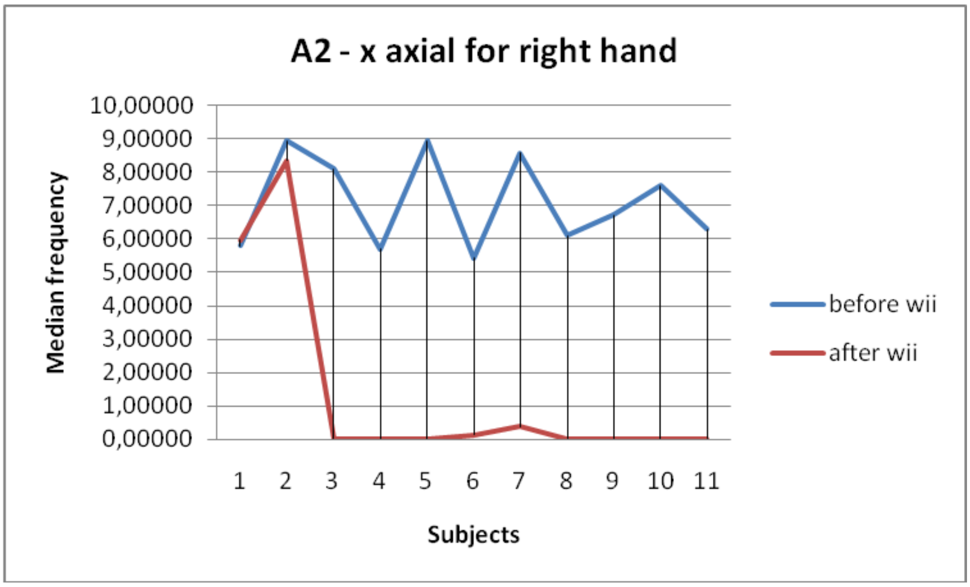


Figure 4.43 Differences in MDF in x axial for right hand during A2 position

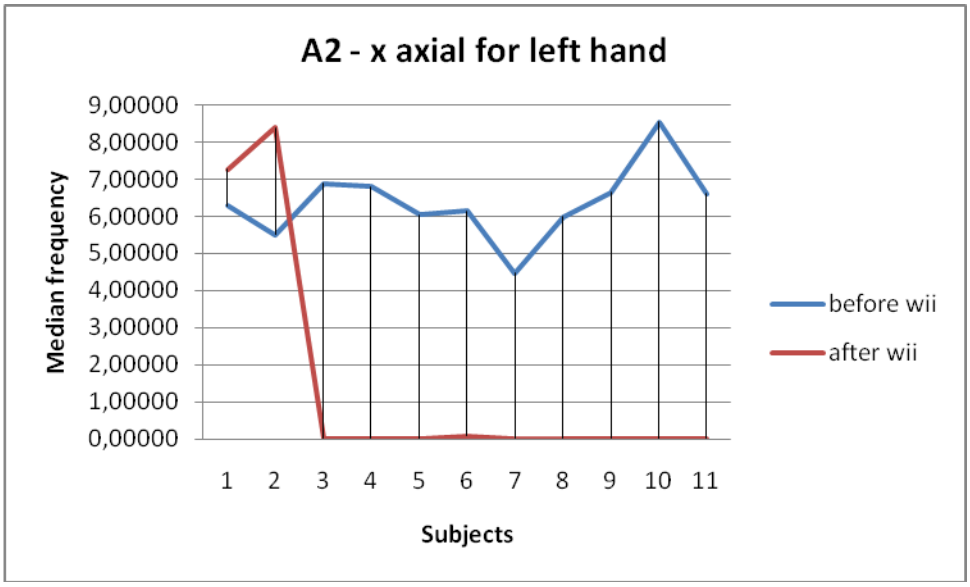


Figure 4.44 Differences in MDF in x axial for left hand during A2 position

4.3.5 Median Frequency on the Y Axial at A2 Position

There were increasing on the right hands of first and second patients, decreasing on the right hands of the other patients (Fig. 4.45). Also, there was increasing on the left hands of first and second patients and decreasing on the left hands of the other patients (Fig. 4.46).

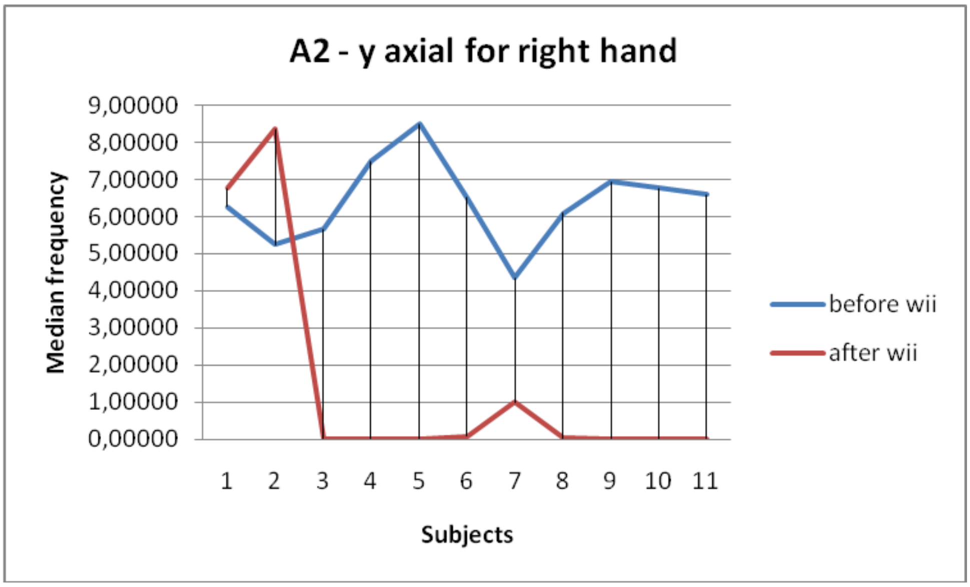


Figure 4.45 Differences in MDF in y axial for right hand during A2 position

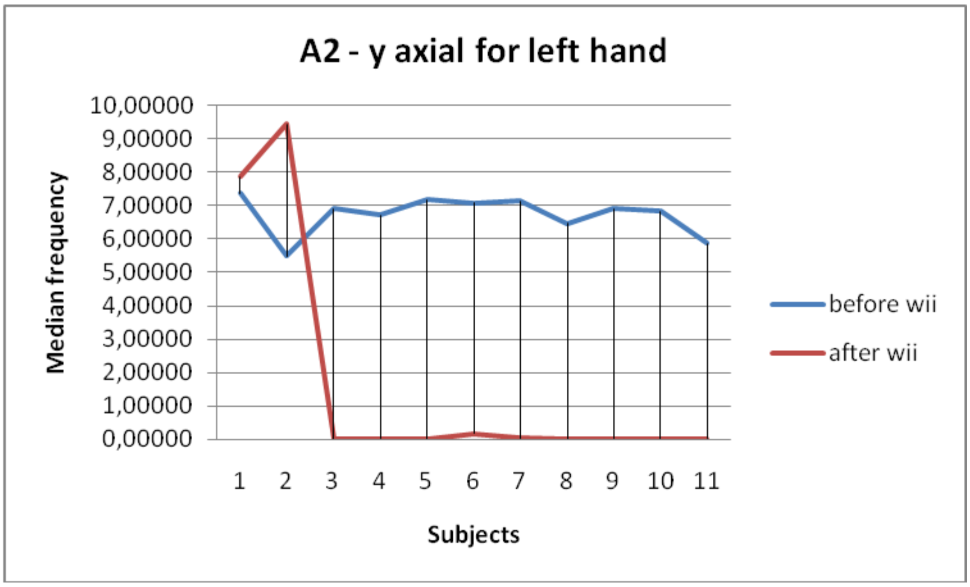


Figure 4.46 Differences in MDF in y axial for left hand during A2 position

4.3.6 Median Frequency on the Z Axial at A2 Position

There were increasing on the right hands of first and second patients, decreasing on the right hands of the other patients (Fig. 4.47). Also, there was increasing on the left hands of first and second patients and decreasing on the left hands of the other patients (Fig. 4.48).

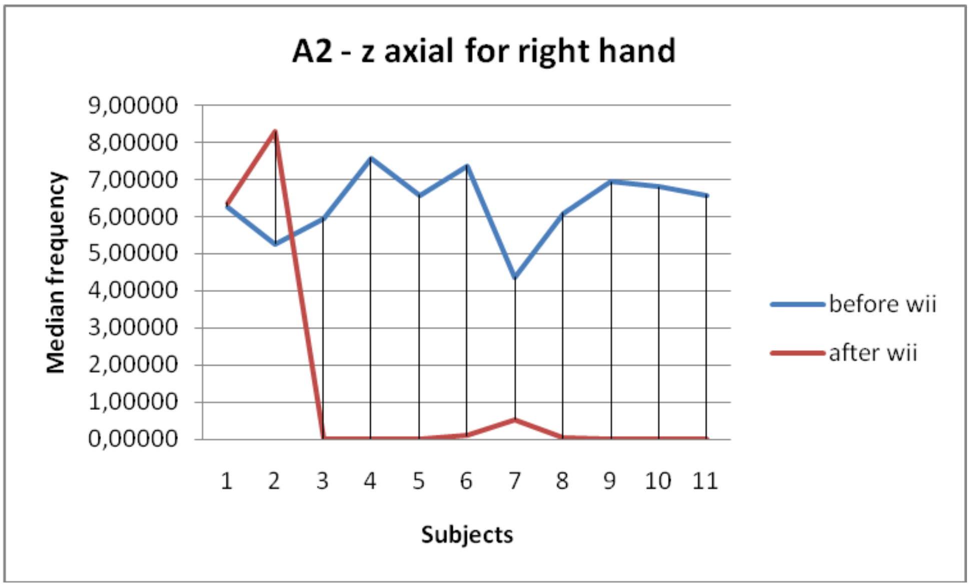


Figure 4.47 Differences in MDF in z axial for right hand during A2 position

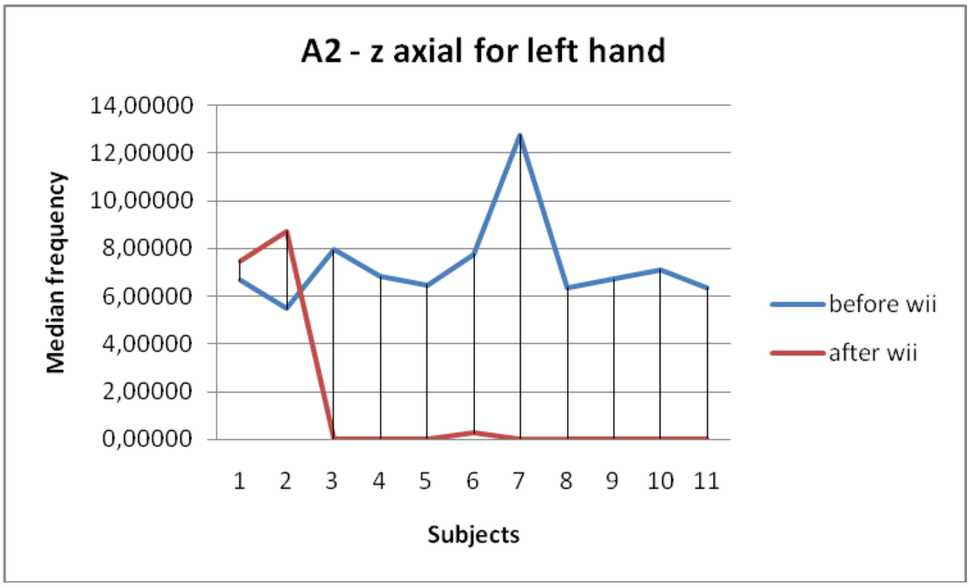


Figure 4.48 Differences in MDF in z axial for left hand during A2 position

4.3.7 Median Frequency on the X Axial at A3 Position

MDF increased on the right hand of second patient and decreased on the right hands of the other patients (Fig. 4.49). Also it increased on the left hand of second patient and decreased on the left hands of the other patients (Fig. 4.50).

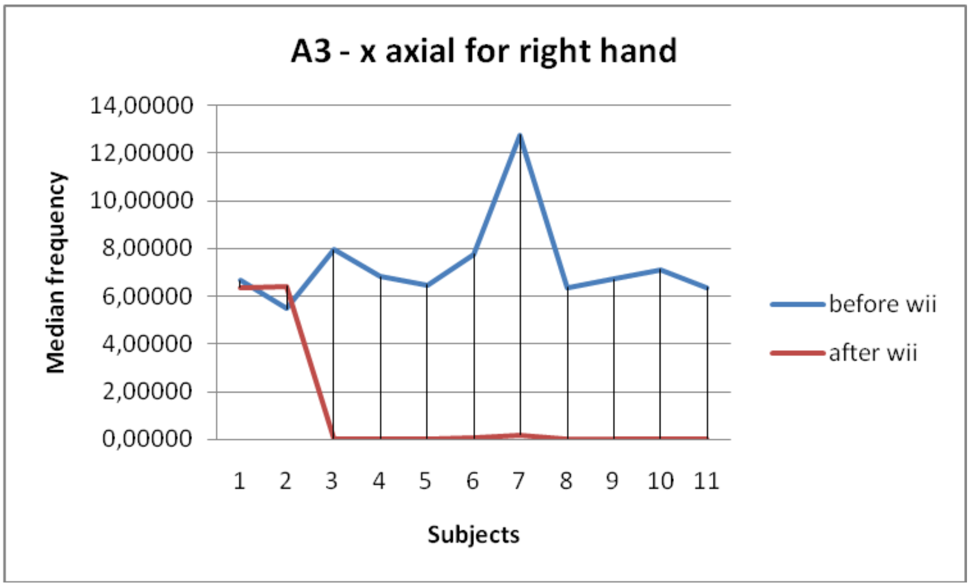


Figure 4.49 Differences in MDF in x axial for right hand during A3 position

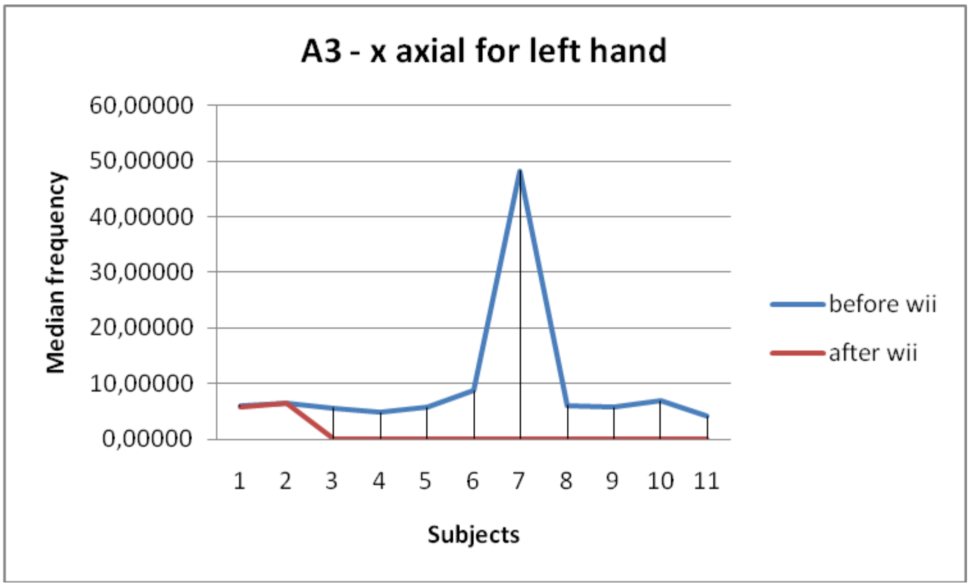


Figure 4.50 Differences in MDF in x axial for left hand during A3 position

4.3.8 Median Frequency on the Y Axial at A3 Position

MDF increased on the right hands of first and second patients, and decreased on the right hands of the other patients (Fig. 4.51). Also it decreased on the left hands of all of the patients (Fig. 4.52).

(Fig. 4.54).

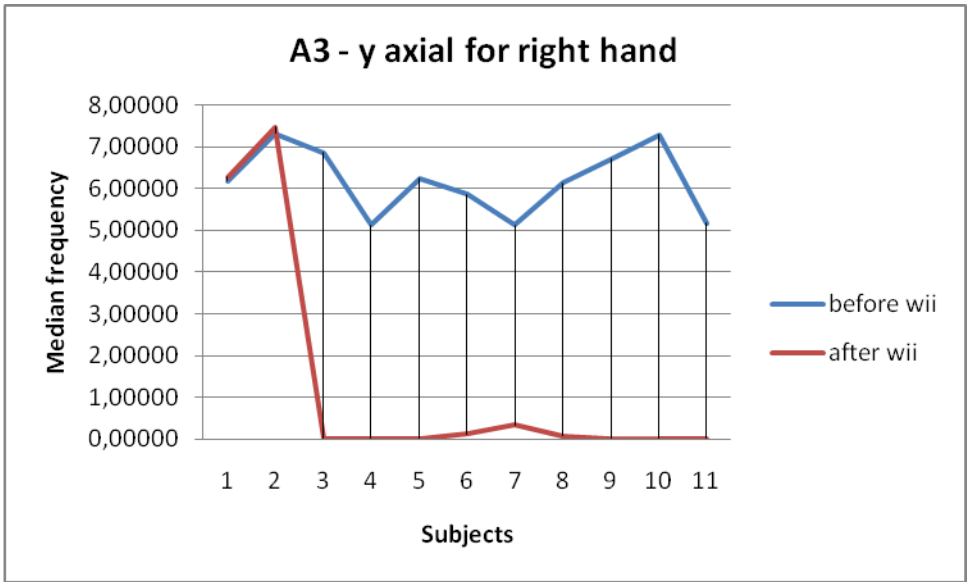


Figure 4.51 Differences in MDF in y axial for right hand during A3 position

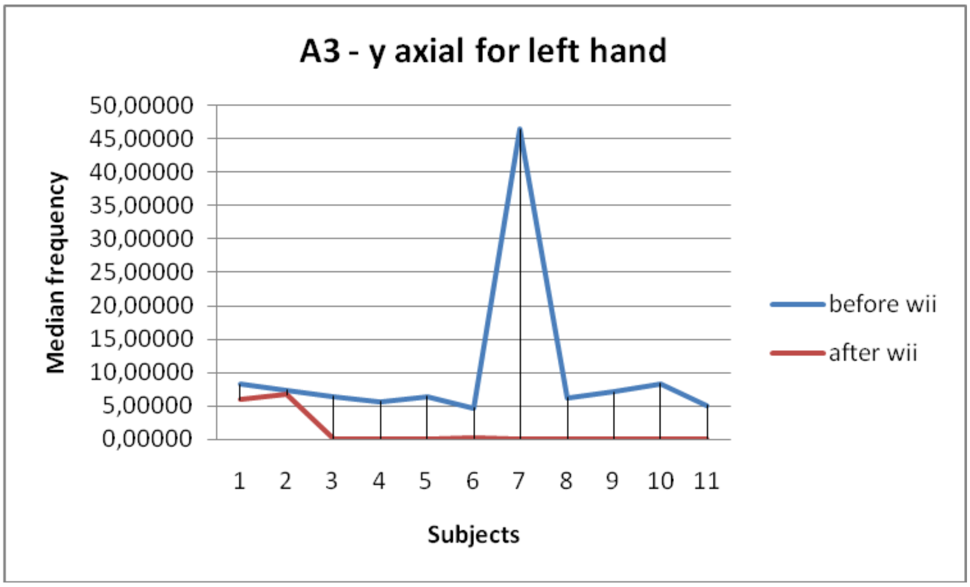


Figure 4.52 Differences in MDF in y axial for left hand during A3 position

4.3.9 Median Frequency on the Z Axial at A3 Position

MDF increased on the right hand of second patient and decreased on the right hands of the other patients (Fig. 4.53). Also it decreased on the left hands of all of the patients (Fig. 4.54).

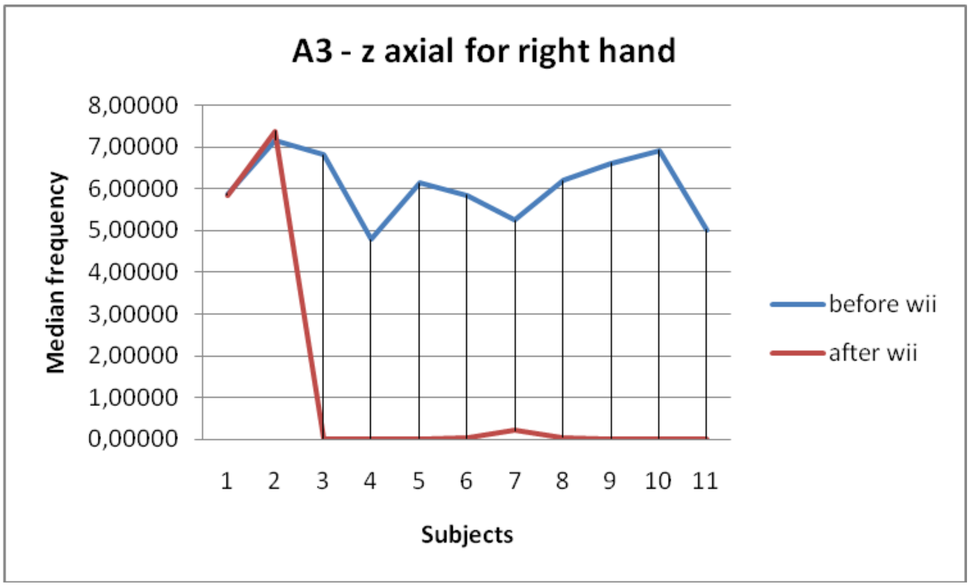


Figure 4.53 Differences in MDF in z axial for right hand during A3 position

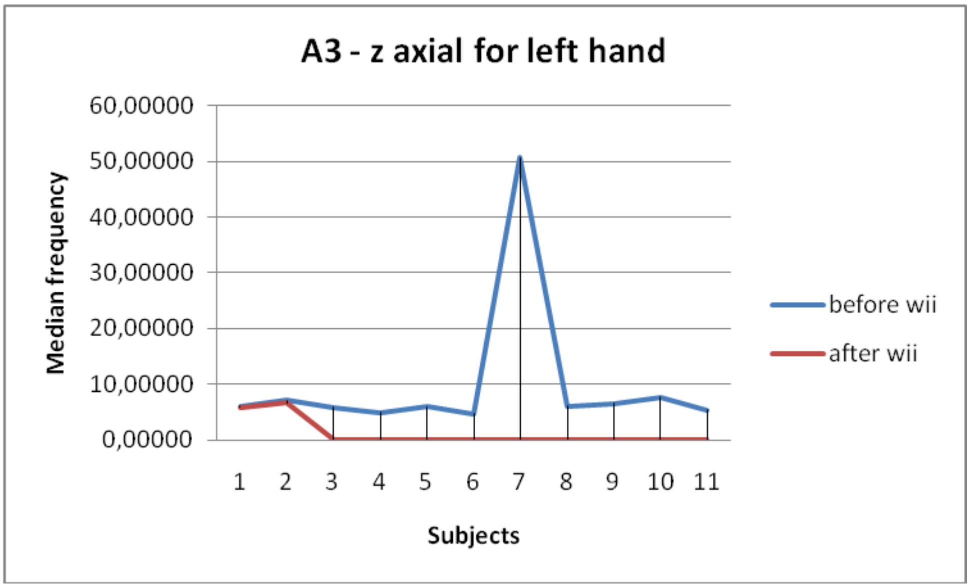


Figure 4.54 Differences in MDF in z axial for left hand during A3 position

When mean variables were evaluated, seen that the MDF decreased on the all of positions and both of right and left hands after wii exercise programme. There were significant differences between the median frequency values of before wii exercise and after wii exercise at the end of the study (Table 4.3).

Table 4.3 Mean and Standard deviation variables of median frequency before wii exercise and after wii exercise

Recording case	Axial and hand	Mean and Standard deviation	
		Before exerxise	After exercise
A1	X axial right hand	6,97049±1,5242	1,29509±2,8634
	X axial left hand	7,04956±0,9204	1,31454±2,9253
	Y axial right hand	7,22157±0,8169	1,40985±3,1206
	Y axial left hand	7,47403±1,3469	1,29415±2,8772
	Z axial right hand	7,03846±0,9699	1,25991±2,8033
	Z axial left hand	7,67101±0,9752	1,39178±30915
A2	X axial right hand	7,10089±1,3589	1,35219±2,9208
	X axial left hand	6,39343±1,1049	1,47737±3,0392
	Y axial right hand	6,34211±0,9244	1,39613±2,9664
	Y axial left hand	6,35875±0,9984	1,43678±3,1699
	Z axial right hand	6,71109±0,5726	1,59299±3,5008
	Z axial left hand	7,30757±1,9315	1,50311±3,2716
A3	X axial right hand	5,62356±1,0302	1,19064±2,5691
	X axial left hand	6,18258±0,8122	1,30404±2,7721
	Y axial right hand	6,05358±0,7897	1,23433±2,6830
	Y axial left hand	9,85302±12,3807	1,12851±2,4711
	Z axial right hand	10,19287±12,0622	1,16592±2,5344
	Z axial left hand	10,10825±13,4776	1,14877±2,5294

DISCUSSION AND CONCLUSIONS

PD is a common neurodegenerative disorder characterized by loss of dopaminergic neurons in the substantia nigra of brain and movement disturbance [31]. There are several clinical manifestions in PD that are defined as motor dysfunctions and non-motor dysfunctions. The main motor signs are tremor, bradykinesia, rigidity, and postural instability [34]. The most common motor symptom is tremor which is seen in PD patients [35]. It is determined as rhythmic and involuntary oscillation of body parts [36]. During treatment the medication is applied to patients [37]. DBS is applied when the drug treatment is not enough for patient. Also during treatment several exercises are adviced to patients for treatment of tremor [38]. A type of these exercise is Wii game console that is produced by Nintendo Company. Some researchers offer wii exercise to improve tremor symptoms [39].

To prove the positive effect of wii exercise on tremor symptoms scientifically, Wii exercise was applied for 9 weeks and tremor signals was recorded from PD patients. PD patients (N=11; 7 female and 4 male) were diagnosed in Clinics of Neurology in Bezmialem Vakif University Faculty of Medicine and Hospital who were taking same drugs for same duration. Then they were directed to Clinics of Physical Therapy and Rehabilitation for programming their Wii exercise. Subjects participated in Wii exercise programme for nine weeks and they played three different games. Patients moved as step on the Wii Fit balance board during first game duration to improve their lower extremities, during the second game they butted to ball to improve their upper extremities who were sensible for ball which appeared on the monitor. Also, during the last game participants held the Wii remote by one hand and Nunchuck controller by the other hand, and they play boxing to improve their upper extremities. Each of these games durations were ten minutes, so total duration of a train was thirty minutes. It was seen that, patients were successful while playing boxing.

Tremor signals were recorded before Wii exercise programme and at the end of the programme. It is seen that, several device are used to recording tremor signals as helium neon laser, accelerometer, tremor pen, etc. in literature. xyzPlux Accelerometry (Plux-Engenharia de Biosensores, Lda.) was used for recording tremor signals in our study. The electrodes were placed on the metacarpophalangeal joints on the index fingers both of right and left hands of participants and signals were recorded in 3 cases (hands were on the table, hands were in free fall, and during task) and duration of each of cases was 3 minutes. It was observed that, patients were forced during the last recording position.

Recorded tremor signals were analyzed in time domain and frequency domain. There are several tremor characteristics that analyzed in frequency domain as harmonic index, center of mass frequency concentration, harmonic index, etc. in literature. Highest peak and median frequency were analyzed in frequency domain and amplitude was analyzed in time domain which was called tremor intensity in our study. Amplitude values are not enough to evalute tremor, especially low amplitude is not discriminative characteristics of tremor [12]. So frequency domain parameters were analyzed in this study. Instead of FT method, FFT method was used transform recorded signals to digital signals sequences in our study. Because FT method is old and unfavorable for signal analysis [40]. Also frequency domain characteristics' PSD was evaluted with using Welch method.

When we compared the TI, HP and MDF values, decreasing was observed in tremor intensity for some patients' hands. Also decreasing was seen in frequency domain characteristics almost for all patients at the end of the study. Previous studies have shown the frequency of physiological tremor is higher than pathological tremor [27]. So, if tremor intensity decreased and frequency domain parameters increased, we could say Wii exercise has positive effect on tremor in PD patients.

In literature, there are many studies about determining and analyzing tremor characteristics.

Anne Beuter *et al.* aimed to identify the most reliableand discriminative tremor characteristics. They recorded postural tremor (with visual feedback and no visual feedback) and rest tremor (with no visual feedback) signals with using laser. They studied on amplitude (tremor intensity) and seven frequency domain characteristics (dispersion around the median frequency, median frequency, center of mass frequency concentration, highest peak, harmonic index, proportional power in the 4- to 6-Hz range, and proportional power in the 7-to 12-Hz range). According to their evaluating the tremor characteristics they found that the most discriminative feature was median frequency in postural tremor with no visual feedback [27]. They used analog output sensor, whereas in our study we used triaxial accelerometer.

Oscillatory movements can be evaluated not only in two extremities but also can be evaluated in all four extremities as upper limbs and lower limbs. Based on this hypothesis, Blake K. Scanlon *et al.* investigated the properties of oscillatory movements in postural and rest positions for all four extremities in PD patients. They used biaxial accelerometer to record the tremor signals and analyzed three parameters such as tremor intensity, center frequency, and intraindividual variability of center frequency like Anne Beuter *et al.*. At the end of this study they found that patients' tremor intensity was not greater than controls, lower intraindividual variability of center frequency in PD patients versus control was important discriminative feature and mean frequency of oscillation movements was not good discriminative factor [32]. Similar study was confirmed by Anne Beuter *et al.*, they studied on tremor amplitude, tremor frequency, and harmonicity of tremor for characterization [12].

Robert LeMoyne *et al.* aimed to record tremor with using iPhone wireless accelerometer in PD patients. They demonstrated the iPhone wireless accelerometer application can be used for characterizing parkinsonian tremor [33].

Zsuzsanna Farkas *et al.* recorded simultaneously PT signals and ET signals from subjects using accelerometry. Their objective was comparing tremor intensity, center frequency, and frequency dispersion of PT and ET. According to their findings, tremor intensity of PT and ET was higher than control subjects. Center frequency and frequency dispersion in both of PT and ET were smaller than controls [9].

In our study we analyzed time domain and frequency domain characteristics at the end of Wii exercise programme. Contrary to expectation, results were showed that Wii exercise programme has not positive effect on tremor. Because frequency of physiological tremor is seen in 7-to 12-Hz and pathological tremor is seen in 4-to 6-Hz frequency band [27]. But our subjects' variables decreased at the end of the exercise programme. This situation depends on several factors during exercise and recording such as patients' motivation, sleep quality before exercise day and recording day, type of nutrition and time, and other physiological causes. Even it can be affected that, talking during recording.

During the currrent study some patients left off their Wii exercise programme due to suffer from another disease. Finding new participants who suitable for our study took long time. So, statistical test was not applied to data because of few participants. If there were more than participants, more significant results could be obtained.

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