REPUBLIC of TURKEY
DOKUZ EYLUL UNIVERSITY
THE INSTITUTE of HEALTH SCIENCES

Alterations in Lower Extremity Muscle Activation and Joint Angle Patterns During Gait in Patients with Type 2 Diabetes Mellitus with and without Polyneuropathy

by

MSc. PT. Duygu ILGIN

Ph.D. in Physical Therapy and Rehabilitation

Ph.D. Thesis

İZMİR-2007

REPUBLIC of TURKEY
DOKUZ EYLUL UNIVERSITY
THE INSTITUTE of HEALTH SCIENCES

Alterations in Lower Extremity Muscle Activation and Joint Angle Patterns During Gait in Patients with Type 2 Diabetes Mellitus with and without Polyneuropathy

Ph.D. in Physical Therapy and Rehabilitation

Ph.D. Thesis

by

MSc. PT. Duygu ILGIN

First Supervisor: Assist. Prof. Salih ANGIN
Second Supervisor: Assist. Prof. H.H.C.M. SAVELBERG

(This research was carried out with Socrates-Erasmus Student Exchange Program at Maastricht University, Faculty of Health Science, Department of Human Movement Science, in the Netherlands.)

THESIS EXAMINATION RESULT FORM

We have read the thesis entitled **"Alterations in Muscle Activitation and Joint Angle Patterns During Gait in Patients with Type-2 Diabetes Mellitus with and without Polineuropathy"** completed by MSc. PT. Duygu ILGIN under supervision of Assist. Prof. Salih ANGIN and Assist. Prof. H.H.C.M. SAVELBERG and we certify that in our opinion it is fully adequate, in scope and in quality, as a thesis for the degree of doctor of philosophy.

Assist. Prof. Salih ANGIN
Chairman

Prof. Dr. Sena YEŞİL
Committee Member

Assoc. Prof. Mehtap MALKOÇ
Committee Member

Assist Prof. Hans H.C.M. SAVELBERG
Jury Member

Assoc. Prof. S. Ufuk YURDALAN
Jury Member

Assoc. Prof. Ayşe ÖZCAN EDEER
Jury Member

Assist. Prof. Nihal GELECEK
Jury Member

CONTENTS

Page Number

TABLE LIST

PICTURE LIST

ABBREVIATIONS

DM	Type 2 Diabetes Mellitus
DPN	Diabetic Polyneuropathy
DC	Diabetic Controls (Subjects With Type 2 Diabetes Mellitus Without Polyneuropathy)
HC	Healthy Age-Matched Controls
mmol/l	millimol/liter
VPT	Vibration Perception Thresload
V	Volt
EMG	Electromyography
Gm	m. Gastrocnemius Caput Medialis
S	m. Soleus
GS	m. Gastrosoleus
TA	m. Tibialis Anterior
VM	m. Vastus Medialis
BF	m. Biceps Femoris
RF	m. Rectus Femoris
GM	m. Gluteus Maximus
Hz	Hertz
mV	milivolt
Sec	Second
ms	Millisecond
m	Meter
m/s	Meter/second
BMI	Body Mass Index
Kg	Kilogram
%	percentage
◦	Degree
LSD	Least-Significant Difference

ABSTRACT

Alterations in Lower Extremity Muscular Activation and Joint Angle Patterns During Gait in patients with Type-2 Diabetes Mellitus with and without Polyneuropathy

Duygu ILGIN, PT, MSc.
Dokuz Eylül University the Institute of Health Sciences, IZMIR/TURKEY

Aim: The aim of this study was to determine Type 2 Diabetes Mellitus (DM) and Diabetic Polyneuropathy (DPN) related lower extremity muscle activation and joint angle alterations independently from the gait speed.

Material and Methods: 10 Type 2 DM, 8 DPN and 10 healthy age-matched subjects were evaluated at a comfortable and a test speed of 1.4 m/s. Gait characteristics, muscular activation characteristics and joint angle characteristics for the ankle, knee and hip joints were determined.

Results: It has been determined that gait speed is lower (p=0.374) and relative duration of stance phase is higher (p=0.433) in DPN group subjects. It has been found out that m. tibialis anterior off time is delayed (p=0.022), m.vastus medialis activation amplitude is lower (p=0.045), activation duration is longer (p=0.028) in DPN group subjects at test gait speed. Knee joint range of motion (p=0.048) and maximum knee joint extension angle is smaller (p=0.076) in DM and DPN group subjects.

Conclusion: Our study has shown that when the gait speed has been standardized, lower extremity muscular activation changes at the ankle and knee joint levels in DPN, and the joint angle differences at the knee joint level in relation to DM and DPN emerge during the early period of the stance phase. It is obvious that these changes will cause some impairments in braking force capacity while transfering the body weight from the heel to the forefoot gradually during gait.

Keywords:Type 2 Diabetes Mellitus, Diabetic Polyneuropathy, Electromyography, Gait Analysis

PREFACE

Sensory, motor and autonomic affection related with Type 2 Diabetes Mellitus (DM) and Diabetic Polyneuropathy (DPN) causes changes in gait characteristics by preventing the creation of proper motor control strategies.

These changes restrict the mobility level of the individual accompanying the postural instability and balance problems, increase in the risk of fall, deviations from the normal pressure distribution, development of plantar pressure ulcers, increase in the infection risk and lower extremity amputations in various levels. This restriction causes decrease in quality of life and functional independence level of DM and DPN subjects. That is why, the determination of changes that may develop in neuromuscular system due to DPN and DM is crucial in the creation of protective and therapeutic approaches aiming at the maintenance and development of the gait performance that is one of the most important indicators of the functional capacity in DM and DPN subjects.

It is stated that the affection developed in muscular function due to DM and DPN may cause the changes in the gait characteristics. In the previous studies, the basic issues evaluated are muscular activation changes related to m. tibialis anterior, m. gastrosoleus, m. quadriceps femoris, hamistring muscles and joint angle changes related to ankle and knee joints. However, although it is known that gait speed is a factor affecting muscular activation and joint angle parameters, this fact has been ignored in the studies carried out to evaluate the muscle activation and joint angle changes related to DM and DPN cases who have been shown to have a lower gait speed when compared with healthy control group subjects.

That is why our study has been carried out by evaluating the subjects at the same gait speed in order to be able to determine the DM and DPN related lower extremity muscle activation and joint angle pattern alterations independently from the gait speed.

1. INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a chronic endocrine disease causing impairments in neuromuscular system. It affects the 5-7% of the world population. According to World Health Organization, while 135 million people suffer from DM in 1995, 300 million people will suffer from this illness and its complications in 2025 (1).

Diabetic Polyneuropathy (DPN) is the most common and the most important complication of the DM. (1-3). It causes sensory, motor and autonomic affection advancing from distal to proximal depending on the duration and severity of hyperglycemia (1-9). Both increasing DM incidence and extended human life increase the frequency and effects of neuromuscular impairments caused by DM and its long term complication DPN (6, 9, 10).

When the gait characteristics of the DM and DPN subjects have been compared with the control group subjects, it has been shown that while gait speed, step and stride length, swing phase duration, joint torque and ground reaction forces are lower, stance phase duration and step width are higher (5-8, 11-14). It has been suggested that gait strategy changes from ankle strategy to hip strategy in accordance with the changes indicated above (11). These changes restrict the mobility level of the individual accompanying the postural instability and balance problems, increase in the risk of fall, deviations from the normal pressure distribution, development of plantar pressure ulcers, increase in the infection risk and lower extremity amputations in various levels (5-10, 13-23). This limitation causes a decrease in the quality of life and functional independence level of DM and DPN subjects (3, 24).

It has been thought that impairments in neuromuscular system components in relation to DM and DPN are the factors underlying these changes determined in gait characteristics. Because gait emerge as a result of the harmonic interaction between neural and muscular structures. Any impairment in any one of these structures will affect the gait characteristics which is a dynamic function (5-8, 12, 14, 25, 26). It has been thought that the impairments arising in the muscular function in relation to DM and DPN may cause changes in the gait characteristics (27-30). The existence and severity of DPN in addition to DM makes these distal to proximal advancing changes in muscle function more apparent (4, 9, 26).

Since the plantar area is the first area on which the first contact with the ground has been provided, it plays an important role in the transfer of sensory stimulus to the nervous system. Motor responses which are created in this way develop the normal gait pattern (6, 21, 31, 32). However, the affection in tactile, vibration, proprioception and kinesthesia senses prevents the creation of proper motor responses and causes anormal gait patterns by advancing from distal to proximal in DM and DPN subjects (8, 33). Therefore, studies about muscular activations have majored on the ankle joint level. The most fundamental muscles that have been determined to be affected in relation the sensory and motor affection at the ankle joint level are m. tibialis anterior (TA) and m. gastrosoleus (GS)(6, 27-29).

In DPN subjects, it has been shown that there is a delay in the parameters such as the activation on-off time, contraction time, maximum activation peak time and activation duration has extended (6, 27-29). These changes were associated with fibular nerve affection which is the first first nerve affected related to DPN (6, 15). Although it has been shown in the studies of Abboud and Sacco that the activation of GS is delayed without being statistically significant, Kwon et al. showed that the activation on time and duration of this muscle are earlier than the healthy group subjects (6, 27, 28). It has been suggested that early GS activation can be related to early plantar flexion moment and the low dorsiflexion moment. It has also been defended that the peak plantar flexion moment which is lower than those of healthy controls may have developed in relation to two factors.These two factors are the incerase in the need for safer walking (12-14) and the decrease in plantar flexor muscle strength due to DPN (26). Gutierrez et al. stated that fast ankle torque creation capacity decreases in the subjects having similar muscle strength and this change may depend on distal denervasion in type-2 fast twitch fibers (25). It has been indicated that TA-GS cocontraction increases depending on the increased stability need in relation with DM and DPN (28-29). The restriction in ankle mobility accompanies these muscular activation changes (30).

The muscle groups for which the changes in the muscular functions in relation to DPN in the knee joint level have been shown as a seconder to the sensory and motor deficiencies which move from distal to proximal are m. quadriceps femoris and m. hamistrings (6,28,29). While, Sacco et al. determined that m. vastus lateralis activation peak delayed due to sensory affection and that is why impairments may develop during the weight transfer to the lower extremity, Kwon et al. determined that the activitations of m. vastus medialis and m. hamstring medialis start early, off times delayed, activation durations extend, and vastus

medialis-medial hamstring cocontractions increased (6, 28). These activation changes are consistent with the low peak knee extension moment results (28). However, Mueller et al. found out that there is no difference among groups with respect to knee extension moment (11). Andersen et al. indicated a decrease in knee extansor muscle strength (%7) and knee flexor muscle strength (%14) (26). When the joint angle changes were evaluated at knee joint level, it has been determined that maximum knee angle decreases (13).

Mueller et al. states that impairments at the ankle joint level are compensated by the increased activation at the hip joint level. However, it has not been shown yet (11).

As a result, in these studies it has been asserted that sensory, motor and autonomic affection in DPN group subjects causes impairments at ankle and knee joint levels during the early and late periods of stance phase. These changes restrict the mobility level of the individual. In accordance to these changes, it has been suggested that these will trigger off changes in the plantar pressure distribution and may lay a groundwork for the growth of plantar pressure ulcers causing an earlier weight transfer to the front of the foot and an overmuch weight lay on the knee joint (6, 27-29).

However, Petrofsky et al. have shown that similar changes have occured in the TA and GS muscle groups at early and late terms of the stance phase, and in the m. quadriceps femoris and m. hamistrings in the knee joint level with the DM group subjects for whom any kind of sensory and motor loss have not been determined. They also shown that there is an increase in the flexion, extension and lateral movements which have been determined with accelerometer belonging to the lower extremity joints. It has been thought that at this point some other factors might be effective besides the changes related to sensory and motor loss. Petrofsky et al. have defended that the visual and vestibular impairments which are connected to microvascular affection developing as a seconder to hyperglicemia might trigger off these changes (29).

However, in the studies in which muscular activations and joint angle changes belonging to DM and DPN subjects for whom the gait speed they perform have been shown lower than those of the healthy control group subjects are examined, the gait speed effect has been ignored.

Many gait characteristics are affected by the gait speed. Muscular activation determined using EMG and joint angles that is a product of muscular activation are two of the factors that are affected by the gait speed (34-41). Lower extremity muscles have the ability of adapting

the changes in gait speed. Because of this adaptation ability, neuromuscular system has the ability of responding the changing conditions and needs. Increase in gait speed causes increasing muscular activation bacause of the increasing muscular strength need. Joint angles emerged depending on the muscular activation are affected in accordance with the step characteristics changing depending on the speed and the increasing need of shock absorption during the contact between the extremity and the ground (36). That is why during the gait analysis, gait speed effect that may emerge in muscular activation and joint angle parameters should be considered. The evaluations carried out in this way can show the the changes specific to patalogy. That is why, gait speed should be standardized (42-45).

Only Kwon et al. have suggested that, speed factor might have some effects on joint moment and muscular activation parameters, and they determined that the peak hip extension moment and m. soleus activation off time in DPN subjects are correlated with gait speed. However, as in the other studies, DPN subjects have been evaluated at a speed which is lower than the healthy group subjects and is chosen by the subjects themselves and the gait speed was not standardized (28).

Based on this information, the hypothesis, "the changes in lower extremity muscular activation and joint angle patterns related with DM and DPN will be exhibited by investigating these changes independently from the gait speed effect" has been suggested.

In accordance with this hypothesis, our study has been carried out by investigating the DM, DPN and age-matched healthy control group subjects at same gait speed to determine the alterations in lower extremity muscular activation and joint angle patterns related with DM and DPN independently from the gait speed.

For each parameter, the following questions have been tried to answer:

- The effect of gait speed independent of DM ve DPN effect,
- DM and DPN effect independent of gait speed effect, and
- The existence of interaction between gait speed effect and DM-DPN effect.

2. MATERIALS-METHODS

2.1. Subjects

In this study 28 subjects were recruited to take part, they were divided in three groups: subjects with diabetic polyneuropathy (DPN), diabetic controls (DC) and healthy age-matched controls (HC; Table 1).

Table 1. Subject Characteristics

	DC (n=10)	DPN (n=8)	HC (n=10)	p value	Post-hoc LSD (p)
Age (years)	60.50±6.95	68.88±5.79	72.40±5.99	0.001*	0.010* 0.000** 0.249
Weight (Kg)	81.30±13.25	84.13±10.90	71.50±10.03	0.063	0.610 0.069 0.029***
Height (m)	1.67±0.10	1.73±0.06	1.70±0.07	0.256	0.102 0.397 0.386
BMI (Kg/m²)	29.24±3.74	27.98±3.17	24.75±2.87	0.016*	0.425 0.005** 0.049***
Vibration Perception Thresload(V)	17.85±6.66	38.13±8.37	24.60±11.92	0.000*	0.000* 0.118 0.005***
Right Leg Length(m)	0.77±0.08	0.82±0.04	0.78±0.06	0.285	0.122 0.621 0.270

Values are mean ± standart deviation.

*** Statistical significance between groups, p<0.05.**

*** Statistical significance for Post-hoc LSD between DC and DPN, p<0.05.**
**** Statistical significance for Post-hoc LSD between DC and HC, p<0.05.**
***** Statistical significance for Post-hoc LSD between DPN and HC, p<0.05.**

The two groups of diabetic subjects were recruited from a database of the department "Internal Health" (Dr. N. Schaper) at the Academic Hospital of Maastricht. The healthy elderly control subjects were recruited from an existing database at the Department of Human Movement Science of the Universiteit Maastricht. This study was approved by the Local Ethics Committee of Maastricht University Hospital, Maastricht, The Netherlands(Appendix 1). Prior to the start of the trial sessions all subjects have been informed about the tests and they signed an informed consent form (Appendices 2-3).

2.2. Subject Selection Criteria

2.2.1. Inclusion Criteria:

The first inclusion criterion for diabetic patients was the diagnosis of type 2 diabetes under stable metabolic control. The subjects were included when they could walk independently without pain and without an assistive device. The blood glucose concentration had to be between 5 - 16 $^{mmol}/_{liter}$ during the test trials. If these concentrations would turn out to be lower or higher, the results of the measurements might be affected and besides passing these extreme values could be of risk to the subjects. In this study, it was not necessary to cancel a test session because of extreme blood glucose levels.

2.2.2.Exclusion Criteria:

Subjects were excluded if they had foot deformities, active ulcerations or previous amputations on the plantar surface of the feet. Further on, subjects with severe restrictions of joint mobility in the legs, heart problems, a Body-Mass Index (BMI)>35, or orthopedic or neuromuscular disease other than diabetic neuropathy were not allowed to participate.

2.3. Study Protocol

Subjects wore shorts, a T-shirt, and walked barefoot. Age, sex, weight, standing height, length of the right leg, and peripheral sensation of the subjects were assessed. The length of the right leg was quantified by measuring the distance between trochanter major and malleolus lateralis in upright position. Peripheral sensation was quantified by measuring Vibration Perception Threshold (VPT) in the big toe, using a biothesiometer. The probe of the biothesiometer was held perpendicular to the top of the big toe while the researcher gradually increased the amplitude of vibration. VPT was defined as the amplitude of vibration at the torque the subject first perceived the vibration. The overall score of VPT was calculated from the mean of 10 trials. In case subjects were not able to detect any vibration, a score of ">50" was assigned to the VPT (46).

After determination of subject characteristics retroreflective markers were placed on the subject's right side on the following anatomical landmarks: lateral border of the fifth metatarsal head, tuber calcanei, lateral malleolus, lateral femur condyle, and greater trochanter (Picture 1 (A)). Body positions in the sagittal plane were recorded using a 2-D digital optical recording system, which consisted of a 25 Hz interlaced digital video camera (50 fields/second) (MX5, Adimec, Holland) with a 12,5 mm lens (Ernitec). Recordings were made of two reflective markers on the support surface and five markers on anatomical landmarks of the right leg. Video images were stored on a computer via an 8-bit frame-grabber (DMA magic, Matrox, UK, 512x512 pixels), programmed with DMA Magic (DIFA measuring systems, Breda, Holland). These measurements provided information about gait speed, positions of body segments, range of motion in the joints, angular velocities and accelerations of the joints.

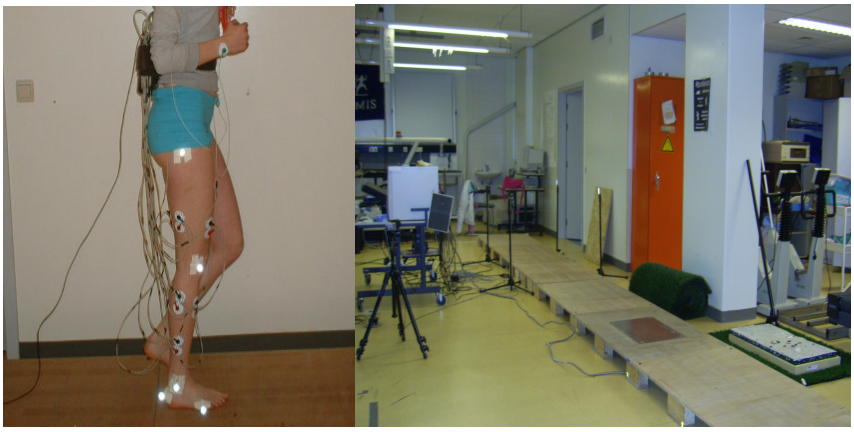
Activity of major muscle groups involved in walking was recorded using a surface electromyographic (EMG) set-up consisting of SPA 20/12 pre-amplifiers (K-lab, Amsterdam, the Netherlands) directly mounted on top of disposable electrodes (CMRR>110dB;input impedance >500 MΩ; signal amplification 100; noise referred to input<2μV_{rms}). The amplifier used was a K-lab MF-118 amplifier (K-lab, Amsterdam, The Netherlands). Signals were A/D (12 bits) converted and all data was stored on a PC with data-acquisition equipment and were synchronised with the digital camera. EMG signals during walking were transmitted by an 8-channel cabling unit. Raw EMG signals were collected from bipolar surface

electrodes containing circuitry for pre-amplification using two chloride electrodes. The diameter of the electrodes was 8 mm, and the inter-electrode distance was 20 mm. Seven EMG electrodes were attached to the belly of the muscles of interest, with the long axis of the electrode positioned parallel to the muscle fibers. All electrode placements were performed using the surface EMG for a non-invasive assessment of muscles recommendation (47). And the correct placements were checked by manual tests and voluntary contractions. Electrodes were placed on *m. gastrocnemius caput medialis (Gm), m. soleus (S), m. tibialis anterior (TA), m. vastus medialis (VM), m. rectus femoris (RF), m. biceps femoris (BF), and m. gluteus maximus (GM).* A reference electrode was put on the right wrist the EMG electrode cables were attached to the leg with anti-allergic tape to avoid problems with the sampling of the images or the walking movement (Picture 1 (A)).

Under two gait speed conditions, subjects walked along a 12m walkway with an imbedded force platform (Kistler Type 9281A) (Picture 1 (B)). During the first condition the subjects walked at a self-selected pace, and during the second condition they were instructed to walk at a test speed [1.4 ms^{-1}].

Prior to data collection of each condition the subjects were allowed to practice trials to get familiar with the equipment and to make sure that they could step onto the force platform with the right foot successfully without targeting.

For each condition five walking trials were recorded. Recording started by pressing a synchronization trigger right after the subject started walking. Duration of data acquisition was five seconds. A successful trial was defined as one in which the subject landed fully on the force platform and speed was 1.4 ms during the second condition.



Picture 1. (A) Positions of the Reflective Markers and EMG Electrots (B) 12 m Walkway with an Imbedded Force Platform

2.4.Data Analysis

The average forward velocity of trochanter major marker was calculated as the gait speed (meter/second, m/s). Stride duration was calculated from the time between subsequent peaks in the EMG signal of the m. gluteus maximus (millisecond, ms). Stance phase duration was defined as the time of contact of the foot with the force platform (ms). Relative duration of stance phase was calculated by the ratio of stance duration to stride duration (percent,%). For all data the time was normalized to the duration of the stride duration.

2.4.1. The Angles of the Ankle, Knee And Hip Joints

Cartesian co-ordinates of the reflective markers derived from the video records were used to calculate hip, knee, and ankle joint angles for a single step cycle using a similar procedure as Winter (1990) (48). For the hip joint, the joint angle defined as the angle between the vertical and the line that connects greater trochanter-lateral femur condyle markers, maximal extension has been determined as maximal hip angle, maximal flexion has been determined as minimal hip angle. The knee joint was defined by the line that connects greater and the lateral femur condyle markers and the line that connects lateral femur condyle and the lateral malleolus markers. Maximal knee joint extension has been determined as maximal knee joint angle, maximal flexion has been determined as minimal knee joint angle. For the ankle joint, by considering the angle between the line that connects lateral malleolus-tuber calcanei and the line that connects tuber calcanei-lateral border of the fifth metatarsal head, maximal plantar flexion and maximal dorsiflexion were determined as maximal ankle joint angle and minimal ankle joint angle, respectively. Joint angles were reported as degree (◦).

2.4.2. Electromyographic Analysis

The raw EMG data were rectified using a 4th order butterworth filter, with a cut off frequency of 10 Hz EMG data were filtered. Muscles were considered active if the EMG value was above 20% of the maximal EMG. Subsequently, the following variables were calculated for each muscle:

The ratio of muscle activity to stride duration: The time that a muscle was active divided by the stride duration (%).

On-off time: Muscle activation beginning and ending time were determined as on-off time for each muscle (ms).

On time: The time as percentage of the stride duration when a muscle is active (%).

EMG amplitude: The peak activation magnitude were determined at EMG amplitude. The ratio of EMG amplitude was determined by the ratio of comfortable peak EMG amplitude to the test peak amplitude (millivolt, mV).

The ratio of coactivity to stride duration: At the hip, knee and ankle joint the relative duration of coactivation was calculated. The time that antagonists at a joint were simultaneously active divided by the stride duration (%).

2.5.Statistical Analysis

For each subject, variables were averaged over the measured trials, with a minimum of three trials. Outliers, defined as group mean ± >2x standard deviation, were excluded from further analysis. These mean values were entered into the statistical program SPSS 11.0 for Windows. Statistical analyses of gait speed, stride-stance duration, relative duration of stance phase, EMG, and joint angle variables were performed using a two-way repeated measures analysis of variance, with gait speed conditions as a two-leveled within subjects factor, and the three groups as between subjects factor. Statistical analyses of subject characteristics and the ratio of EMG amplitude were performed using one-way analysis of variance. A level of significance of $p<0.05$ was chosen. Post-hoc tests were used to locate individual differences. When the results of the analysis were significant ($p<0.05$), the LSD (Less Significance Differerence) post-hoc test was run.

4. RESULTS

3.1. Subject Characteristics

On the average DC participants were 10 years younger than DPN and HC subject ($p<0.001$; Table 1). Healthy controls had a significantly smaller BMI than the other participants (Table1). Body mass, length and length of the right leg did not differ between the groups. Sensibility of the plantar surface turned out to be significantly more affected in the DPN group compared to the DC ($p=0.000$) and the HC group ($p=0.005$).

Table 1. Subject Characteristics

	DC (n=10)	DPN (n=8)	HC (n=10)	p value	Post-hoc LSD (p)
Age (years)	60.50±6.95	68.88±5.79	72.40±5.99	0.001*	0.010* 0.000** 0.249
Weight (Kg)	81.30±13.25	84.13±10.90	71.50±10.03	0.063	0.610 0.069 0.029***
Height (m)	1.67±0.10	1.73±0.06	1.70±0.07	0.256	0.102 0.397 0.386
BMI (Kg/m²)	29.24±3.74	27.98±3.17	24.75±2.87	0.016*	0.425 0.005** 0.049***
Vibration Perception Thresload(V)	17.85±6.66	38.13±8.37	24.60±11.92	0.000*	0.000* 0.118 0.005***
Right Leg Length(m)	0.77±0.08	0.82±0.04	0.78±0.06	0.285	0.122 0.621 0.270

Values are mean ± standart deviation.

*** Statistical significance between groups, $p<0.05$.**

*** Statistical significance for Post-hoc LSD between DC and DPN, $p<0.05$.**
**** Statistical significance for Post-hoc LSD between DC and HC, $p<0.05$.**
***** Statistical significance for Post-hoc LSD between DPN and HC, $p<0.05$.**

3.2. Gait Speed

No significant differences in gait speed were found between 3 groups. Within each group, difference between first and second gait speed was significant (p=0.000; Table 2). All subjects walked slower at first gait speed than at second gait speed.

Table 2. Gait Speeds of the Groups

	DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect (p)	Speed*Group Interaction p)	Group Effect (p)
Gait Speed (m/sn)						
1.Speed	1.06±0.13	1.02±0.14	1.18±0.22	0.000*	0.233	**0.374** 0.565 0.389 0.171
2. Speed	1.41±0.18	1.37±0.15	1.41±0.17			
1./2.Speed	0.76±0.09	0.75±0.11	0.83±0.12			**0.192** 0.248 0.949 0.261

3.3. Temporal Gait Characteristics

Both stance phase duration and stride duration were significantly ($p<0.001$) shorter in the second speed condition (Table 3). None of the temporal characteristics differed between groups.

Table 3. Temporal Gait Characteristics

	DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect p value	Speed*Group Interaction p value	Group Effect p value
Stance Phase Duration (ms)						
1. Speed	698.03±80.53	736.03±114.16	678.95±92.01	0.000*	0.182	**0.732**
						0.668
2. Speed	587.19±58.94	580.72±66.71	581.46±49.91			0.711
						0.435
Stride Duration (ms)						
1. Speed	1126.74±148.42	1152.17±175.78	1107.72±108.07	0.000*	0.356	**0.843**
						0.643
2. Speed	967.96±91.70	898.03±92.63	940.97±72.79			0.599
						0.987
Relative Stance Phase Duration(%)						
1. Speed	62.23±4.07	64.01±5.82	61.14±3.60	0.884	0.632	**0.433**
						0.248
2. Speed	60.79±4.57	64.96±7.94	62.18±7.98			0.949
						0.261

3.4. The Ratio of Muscle Activity to Stride Duration

For most muscles the relative duration of activity was neither affected by gait speed nor by the group considered (Table 4). Exceptions to this rule were found for TA and VM. For TA significant speed and speed*group interaction effects were found, indicating that in both diabetic groups (DC and DPN) the activity lasted longer when the subjects were forced to walk at a velocity of 1.4 m/s. VM was significantly longer active in DPN subjects and under the second gait speed (Table 4).

Table 4. The Ratio of Muscle Activity to Stride Duration

	DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect Pvalue	Speed*Group Interactionp p value	Group Effect p value
M. Gastrocnemius Medialis						
1. Speed	0.45±0.12	0.42±0.10	0.48±0.08	0.118	0.974	**0.490**
						0.530
2. Speed	0.48±0.16	0.44±0.12	0.51±0.09			0.555
						0.238
M. Soleus						
1. Speed	0.49±0.09	0.57±0.09	0.56±0.10	0.318	0.995	**0.121**
						0.078
2. Speed	0.48±0.08	0.56±0.09	0.55±0.11			0.076
						0.875
M.Tibialis Anterior						
1. Speed	0.51±0.06	0.57±0.14	0.55±0.14	0.011*	0.030*	**0.900**
						0.654
2. Speed	0.59±0.10	0.58±0.15	0.56±0.15			0.883
						0.747
M. Vastus Medialis						
1. Speed	0.46±0.11	0.56±0.08	0.39±0.14	0.040*	0.898	**0.028***
						0.158
2. Speed	0.51±0.05	0.58±0.14	0.43±0.15			0.147
						0.008***
M.Biceps Femoris						
1. Speed	0.41±0.16	0.47±0.14	0.38±0.13	0.999	0.799	**0.399**
						0.435
2. Speed	0.42±0.21	0.48±0.18	0.36±0.12			0.523
						0.180
M.Rectus Femoris						
1. Speed	0.39±0.19	0.45±0.14	0.41±0.15	0.460	0.750	**0.588**
						0.311
2. Speed	0.38±0.18	0.49±0.17	0.43±0.20			0.699
						0.495
M.Gluteus Maximus						
1. Speed	0.27±0.09	0.39±0.12	0.34±0.17	0.795	0.231	**0.102**
						0.035
2. Speed	0.24±0.11	0.42±0.16	0.33±0.14			0.213
						0.286

3.5. The Ratio of Coactivity to Stride Duration

When the groups were forced to walk at the test gait speed, it has been determined that coactivation percentage at ankle joint level decreases at DPN subjects while it increases DC and HC group subjects (Table 5).

Table 5. The Ratio of Coactivity to Stride Duration

	DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect pvalue	Speed*Group Interactionp p value	Group Effect p value
Ankle Joint (%)						
1. Speed	0.16±0.08	0.33±0.12	0.26±0.07	0.508	0.028*	**0.203**
						0.089
2. Speed	0.26±0.17	0.26±0.12	0.27±0.11			0.206
						0.552
Knee Joint (%)						
1. Speed	0.62±0.14	0.67±0.15	0.57±0.19	0.526	0.994	**0.410**
						0.516
2. Speed	0.63±0.11	0.69±0.17	0.58±0.20			0.474
						0.189
Hip Joint (%)						
1. Speed	0.41±0.17	0.48±0.18	0.39±0.18	0.326	0.611	**0.339**
2. Speed	0.38±0.18	0.48±0.18	0.34±0.13			0.296
						0.680
						0.152

3.6. Amplitude

It has been determined that VM amplitude is lower in DPN cases when compared with the healthy group subjects (Table 6).

Table 6. EMG Amplitude of the Lower Extremity Muscles

	DC (n=10)	DPN (n=8)	HC (n=10)	Post-hoc LSD p value
M. Gastrocnemius Medialis				
1./2. Speed	0.88±0.25	0.83±0.20	0.99±0.13	**0.275** 0.652 0.275 0.133
M. Soleus				
1./2. Speed	0.81±0.13	0.88±0.09	0.83±0.12	**0.568** 0.307 0.807 0.440
M. Tibialis Anterior				
1./2. Speed	0.81±0.14	0.81±0.11	0.90±0.16	**0.348** 0.971 0.194 0.261
M. Vastus Medialis				
1./2. Speed	0.79±0.19	0.67±0.14	0.88±0.13	**0.045*** 0.157 0.237 0.014***
M. Biceps Femoris				
1./2. Speed	0.76±0.12	0.75±0.12	0.76±0.12	**0.970** 0.813 0.944 0.855
M.Rectus Femoris				
1./2. Speed	0.76±0.15	0.78±0.20	0.74±0.14	**0.926** 0.864 0.833 0.702
M. Gluteus Maximus				
1./2. Speed	0.81±0.24	0.71±0.22	0.81±0.20	**0.690** 0.435 0.983 0.445

3.7. On-Off Time of the Lower Extremity Muscles

In all groups, TA activation on and GM off times are earlier at second gait speed when compared with first one independent of group effect.When the second gait speed is compared with the first gait speed, it has been determined that RF activation off time in DPN subjects is delayed whereas it is earlier in DC and HC group subjects.It has been found that TA activation off time delayed in DPN subjects while VM activation off time delayed in DM and DPN subjects (Table 7).

Table 7. On-Off Time for the Lower Extremity Muscles

		DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect pvalue	Speed*Group Interaction p value	Group Effect p value
M. Gastrocnemius Medialis							
On Time (%)	**1. Speed**	0.07±0.06	0.05±0.03	0.05±0.03	0.709	0.841	**0.442**
On Time (%)	**2. Speed**	0.06±0.08	0.04±0.04	0.05±0.04			0.230
Off Time (%)	**1. Speed**	0.50±0.05	0.50±0.03	0.51±0.03	0.763	0.904	0.348
Off Time (%)	**2. Speed**	0.51±0.05	0.49±0.04	0.50±0.03			0.716 **0.827** 0.555 0.882 0.641
M. Soleus							
On Time (%)	**1. Speed**	0.03±0.03	0.02±0.02	0.02±0.02	0.143	0.063	**0.499**
On Time (%)	**2. Speed**	0.03±0.03	0.01±0.01	0.02±0.03			0.275
Off Time (%)	**1. Speed**	0.53±0.05	0.53±0.03	0.53±0.03	0.249	0.708	0.385
Off Time (%)	**2. Speed**	0.51±0.03	0.53±0.06	0.52±0.04			0.798 **0.663** 0.376 0.710 0.605
M. Tibialis Anterior							
On Time (%)	**1. Speed**	0.59±0.04	0.59±0.04	0.57±0.04	0.000*	0.571	**0.682**
On Time (%)	**2. Speed**	0.55±0.04	0.55±0.05	0.55±0.04			0.923
Off Time (%)	**1. Speed**	0.10±0.02	0.23±0.15	0.13±0.07	0.146	0.118	0.423
Off Time (%)	**2. Speed**	0.12±0.04	0.22±0.10	0.18±0.08			0.515 **0.022*** 0.006* 0.220 0.071
M. Vastus Medialis							
On Time (%)	**1. Speed**	0.89±0.03	0.89±0.04	0.89±0.08	0.290	0.925	**0.941**
On Time (%)	**2. Speed**	0.89±0.05	0.88±0.05	0.88±0.06			0.815
Off Time (%)	**1. Speed**	0.51±0.11	0.47±0.11	0.39±0.14	0.867	0.985	0.739
Off Time (%)	**2. Speed**	0.51±0.04	0.46±0.09	0.38±0.14			0.942 **0.051** 0.415 0.017** 0.135
M. Biceps Femoris							
On Time (%)	**1. Speed**	0.92±0.06	0.90±0.03	0.88±0.06	0.216	0.356	**0.288**
On Time (%)	**2. Speed**	0.91±0.07	0.87±0.04	0.89±0.05			0.221
Off Time (%)	**1. Speed**	0.25±0.10	0.28±0.09	0.25±0.11	0.207	0.385	0.147
Off Time (%)	**2. Speed**	0.22±0.09	0.25±0.08	0.26±0.10			0.911 **0.810** 0.543 0.641 0.835
M. Rectus Femoris							
On Time (%)	**1. Speed**	0.93±0.05	0.90±0.05	0.90±0.04	0.418	0.728	**0.225**
On Time (%)	**2. Speed**	0.92±0.05	0.88±0.05	0.90±0.03			0.090
Off Time (%)	**1. Speed**	0.24±0.14	0.30±0.13	0.24±0.14	0.796	0.014*	0.314
Off Time (%)	**2. Speed**	0.19±0.05	0.37±0.15	0.23±0.14			0.403 **0.160** 0.078 0.823 0.107
M. Gluteus Maximus							
On Time (%)	**1. Speed**	0.95±0.02	0.92±0.07	0.91±0.04	0.393	0.123	**0.401**
On Time (%)	**2. Speed**	0.94±0.02	0.92±0.06	0.93±0.04			0.260
Off Time (%)	**1. Speed**	0.20±0.09	0.28±0.10	0.22±0.08	0.003*	0.204	0.243
Off Time (%)	**2. Speed**	0.16±0.08	0.23±0.11	0.21±0.07			0.912 **0.237** 0.094 0.429 0.295

3.8. Angles of the Ankle, Knee and Hip Joints

With the exception of the maximum ankle joint plantar flexion and maximum knee joint extension angles, all joint angles were significantly affected by gait speed. For ankle and knee joint angles significant speed*group interaction effects were found, indicating that in both diabetic groups the maximum ankle joint dorsiflexion and the maximum knee joint flexion angle increased when the subjects were forced to walk at a velocity of 1.4 m/s. The range of motion of the knee joint was significantly wider in the HC subjects than both diabetic groups ($p=0.048$). The increased range of motion in the HC subjects was caused by less knee joint extension during the initial part of the stance phase ($p=0.076$; Table 8).

Table 8. The Angles of the Ankle, Knee and Hip Joints

	DC (n=10)	DPN (n=8)	HC (n=10)	Speed Effect p value	Speed*Group Interaction p value	Group Effect p value
Ankle Joint (◦)						
1. Speed Minimum	10.53±9.26	15.42±4.23	13.25±4.78	0.001*	0.040*	**0.368**
						0.173
2. Speed Minimum	13.78±9.27	18.18±5.08	13.35±4.95			0.708
						0.290
1. Speed Maximum	31.02±9.46	33.70±6.37	30.76±4.99	0.722	0.628	**0.576**
						0.352
2. Speed Maximum	30.10±10.56	34.18±5.76	30.59±3.70			0.972
						0.358
1. Speed Range of Motion	41.55±18.29	49.12±9.23	44.00±9.28	0.023*	0.190	**0.456**
						0.241
2. Speed Range of Motion	43.87±19.74	52.36±10.27	43.93±7.64			0.838
						0.310
Knee Joint (◦)						
1. Speed Minimum	14.36±5.84	11.82±5.08	9.14±7.26	0.700	0.211	**0.076**
						0.329
2. Speed Minimum	15.10±4.90	11.89±5.44	7.73±5.87			0.025
						0.237
1. Speed Maximum	24.25±4.10	21.04±4.55	23.47±5.60	0.000*	0.025*	**0.375**
						0.193
2. Speed Maximum	28.90±4.71	25.10±4.80	24.54±7.24			0.291
						0.719
1. Speed Range of Motion	9.89±3.45	9.22±4.53	14.13±5.12	0.000*	0.677	**0.048***
						0.744
2. Speed Range of Motion	13.81±3.47	13.22±4.83	16.81±4.28			0.044**
						0.029***
Hip Joint (◦)						
1. Speed Minimum	13.05±5.21	12.77±4.94	17.50±4.71	0.009*	0.861	**0.079**
						0.964
2. Speed Minimum	14.32±5.25	14.81±5.67	18.99±3.89			0.046
						0.067
1. Speed Maximum	24.90±3.54	22.36±1.40	22.93±4.28	0.000*	0.230	**0.214**
						0.150
2. Speed Maximum	27.36±4.22	24.26±2.67	23.70±5.21			0.117
						0.997
1. Speed Range of Motion	37.95±4.07	35.13±5.03	40.43±4.90	0.001*	0.676	**0.159**
						0.246
2. Speed Range of Motion	41.68±4.66	39..06±6.93	42.69±4.77			0.411
						0.058

4.DISCUSSION

Our study has been aimed to identify DM and DPN related lower extremity muscle activation and joint angle changes independently from the gait speed. Our results have shown that lower ekstremity muscle activation changes emerge at the level of ankle and knee joints in DPN subjects, and the joint angle changes emerge at the level of knee joint in DM and DPN subjects during the early stance phase.

At this study, it has been found out that the gait speed is lower (Table 2), and the percentage of the stance phase is higher (Table 3) in DPN group although these results are not statistically significant. It has been thought that these changes which were identified in the gait dynamics are consistent with the sensory loss results obtained from the vibration perception threshold test. The previous studies have also determined that similar changes related to the sensory, motor and autonomic affection exist in the gait dynamics of the DPN subjects (5-8, 11-14).

It is known that gait speed is a factor affecting many kinetic and kinematic parameters such as muscle activation and joint angle (34-41). It has also been shown in our study that this factor caused similar differences with muscle activation and joint angle changes which had been determined to be related to DPN in the previous studies. When the groups are examined with the test gait speed which is higher than the comfortable gait speed, it has been determined independently from the existence of DM and DPN that TA and VM activation durations extend, on-off times of activations pertaining to TA and GM muscles arise early, and joint angle values increase. However, in the studies in which muscle activation and joint angle changes are examined in DPN subjects who have been determined to have lower gait speed than the healthy group subjects, the effect of gait speed has not been considered (6,27,29) Only Kwon et al. have asserted that the speed factor may have effects on these parameters, and identified that the peak hip extension moment and soleus activation off time are correlated with the gait speed. However, the patients of DPN have been evaluated with the comfortable gait speed which is lower than the healthy control group subjects as it was in the other studies (28). Thus, in our study groups have been tested in the same gait speed in order

to be able to observe DM and DPN related muscle activation and joint angle changes independently from the speed effect.

It has been determined that at the ankle level, while TA activation off time of DPN subjects delayed (Table 7); in the test gait speed, the ratio of TA muscle activity to stride duration has increased in each three groups. It has been thought that this delay in the activation off time will cause impairments in the contact of the forefoot with the floor in the stance phase and in the gradually weight transfer onto the lower extremity. Because TA ensures the appropriate position between the foot and the floor with the eccentric contraction following the heel strike during the stance phase, and the weight transfer onto the lower extremity by bringing the tibia forward. This delay that we have determined during the early stance phase is consistent with the delayed contraction time, arising point of maximum activation and, off time which were determined in the studies of Abboud, Sacco, and Kwon et al. (6, 27, 28). Although the gait speed standardization was not provided in these studies, it has been thought that this determination of the similar results with our study and the difference in the TA muscle activation off time may be associated with the DPN. However, increase in activation duration that was asserted by Kwon et al. to arise in the subjects of DPN has been seen in our study in 3 groups with only speed increase independent from the group effects. It can be assumed that this increase depends on the increased lower extremity loading which grows in terms of the speed factor (36).

The second most emphasized muscle group in the previous studies which are related to muscle activation differences at the level of ankle joint is GS. It has been determined by Abbaoud and Sacco et al. that delays have occured in the muscle activations of Gm and S in DPN subjects although it is not statistically significant (6, 27). In our study, a difference in delay among the groups has not been observed. However, it has been observed that GS activation which is not statistically significant in DPN subjects, comes out early similar to Kwon et al. (Table 7). In the study of Kwon, the on time in DPN subjects equals to 2.5% of the stride duration for S muscle and 3.9% for Gm muscle (28). In this study, it has been determined that the on time is, in turn, suitable with the sections of 2% - 1% for S muscle and 5% - 4% for Gm muscle at the comfortable and test gait speed. It has been observed that these times are really earlier when the beginning time of activation which appears in these slices of

stride duration is compared with the on time equaling to the slice of 10% that has been determined for the healthy individuals (48). The early Gs on time is consistent with the increased plantar flexor moment which was determined in the early stance phase in the study of Kwon et al. Despite the lower maximum plantar flexion moment belonging to the term of late stance phase that was determined for DPN subjets by Mueller and Kwon et al., any muscle activation difference has not been determined in our study. It has been assumed that this situation may arise from the low gait speed of DPN group subjects when compared with the healthy control group (11, 28). Although Gs on time showed a tendency to come out early in each 3 groups, it has been determined that this tendency is more appearant in DPN subjects. However, it has been found out that in DM subjects in which any kind of sensory and motor affection has not been found by Petrofsky et al., the activation of GS shows an increase of 5 times more on average when compared with the activation of TA in the early stance phase. This difference has been associated with the existence of microvascular interaction which comes out with the DM (29).

Kwon et al. have demonstrated that there has been a coactivation increase in the levels of ankle and knee joints in DPN group subjects related to somatosensorial deficiency (28). Petrofsky et al. have found a coactivation in these joints even without any sensorial and motor loss (29). The coactivation increase has been associated with the increase in the stabilization need. The difference between these two studies has made people think that there may be some other factors different from the somatosensorial sense loss taking part in the occurance of the coactivation increase. Petrofsky et al. have asserted that this difference might have originated from the microvascular differences arising related to DPN (29). However, Kwon and Petrofsky et al. haven't consider the speed factor in their studies. In our study, although no difference was observed between the groups, when the patients were asked to walk with the same speed, it has been determined that the coactivation percentage determined during the test gait speed has decreased at the ankle level in DPN subjects when it is compared to the coactivation percentage determined during the comfortable gait speed, and showed an increase in both of the control groups (Table 5). It has been thought that this coactivation increase observed as a response to the increasing gait speed has reflected the increased stabilization need arising with the gait speed in accordance with the Petrofsky's results. On

the other hand, the low coactivation percentage in DPN subjects can be related to the TA activation off time arising earlier different from the other groups in the test gait speed.

In our study, the activation differences belonging to the VM which is responsible for the knee extension control have been found in both of the diabetic groups at the knee joint level during the early stance phase (Table 4, 7). However, as affection has been determined in many more parameters in DPN subjects, it has been thought that VM activation differences are basically related to DPN. These results are compatible with the low muscle strength, moment and muscular activation changes belonging to knee extension shown by Andersen, Kwon and Sacco et al. in DPN subjects (6, 26, 28).

The second muscle in which a difference in the activation pattern at the knee joint level has been determined in DPN subjects is RF which helps the function of the vastus muscle group. It has been thought that the activation off time of this muscle was delayed at the test gait speed (Table 7) may have been developed to compensate for the impairments in the activation of VM.

It has been detected that, the dorsiflexion angle of the ankle joint and the flexion angle of the knee joint have increased during the test gait speed in each 3 groups (Table 8). The increases in these angular values are related to the increase in step length which has been detected during the test gait speed which is higher than the comfortable gait speed. It has been determined that in the HC group subjects, range of motion of the knee joint is wider when it is compared to those of DM and DPN subjects (Table 8). It has been thought that this difference is compatible with the inadequate knee extension angle in the DM and DPN groups being consistent to the differences detected during the VM muscular activation.

It can be stated that these differences and the deficiency on the extension angle which have been determined in the activation parameters which belong to the VM and RF muscles at the knee joint level can be regarded as the sign of the deficiency at the knee extension control in the early stance phase related to DPN. It has also been thought that early GS activation belonging to the early stance phase can be an adaptation for the inadequate knee extension. Different from our study, it has been shown with DPN by Abboud, Sacco and Kwon et al.,

and with healthy subjects by Eils et al. that a sensorial loss which was gained by cold immersion and a delay in the GS muscular activation belonging to the late stance phase, activation amplitude, a decrease at the intensity of the second activation peak belonging to ground reaction force have occured and that they also arose early (6, 27, 28, 32). However, during these studies, groups have not been examined in the same gait speed. On the other hand, in the Eils et al., sensorial loss has been created under experimental conditions by using the technique of cold immersion, and vestibular, visual sensorial losses, motor and autonomic affections which may develop due to DM and DPN have been ignored.

It has been asserted by Mueller et al. that the deficiencies originating on the ankle joints related to DPN will be compensated with the increased activation in the hip joint level. However, in our study, it has been determined that muscular activations and joint angle differences have only occured at the ankle and knee joints, but any kind of affection at the hip joint level have not occured. These differences during the activation of TA, VM and RF in DPN subjects and on the angle of knee extension in DM and DPN subjects may lead to the weight transfer to the forefoot at an earlier time. It has been thought that this stuation can cause some differences in the pressure distribution and gait pattern in relation to the decrease in the plantar sense with the healthy subjects as also shown by Eils and Nurse et al. (21, 31, 32).

5.CONCLUSION

Our study has proved that when the gait speed has been standardized, lower extremity muscular activation differences at the ankle and knee joint levels in DPN, and the joint angle differences at knee joint level in DM and DPN subjects emerge in the early period of the stance phase.

It is obvious that these differences will cause impairments in the braking force capacity while transfering the body weight from the heel to the forefoot gradually during the gait. However, for the DM and DPN subjects, with the detailed clinical history, by developing study groups which include more subjects, better explanations of the mechanisms underlying these deficiencies are needed.

The results which will be obtained in this way will be leading for the formation of the protective and therapeutic approaches aiming at the maintenance and development of the gait performance of DM and DPN subjects.

6. REFERENCES

1.Williams G, Pickup JC. Handbook of Diabetes: 3th Edition. Australia, Blackwell Publishing, 2004; 1-168.

2.Witzke KA, Vinik AI. Diabetic neuropathy in older adults. Rev Endocr Metab Disord 2005;6:117–127.

3. Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J 2006;82:95-100.

4.Hiltunen LA. Does glucose tolerance affect elderly persons balance, gait or muscle strength. Cent Eur J Public Health 2001;9(1):22-25.

5.Sacco ICN, Amadio AC. A study of biomechanical parameters in gait analysis and sensitive cronaxie of diabetic neuropathic patients. Clin Biomech 2000;15:196-202.

6.Sacco ICN, Amadio AC. Influence of the diabetic neuropathy on the behavior of electromyographic and sensorial responses in treadmill gait. Clin Biomech 2003;18: 426–434.

7.Petrofsky J, Lee S, Bweir S.Gait characteristics in people with type 2 diabetes mellitus. Eur J Appl Physiol 2005;93: 640–647.

8.Menz HB, Lord SR, St George R, Fitzpatrick RC. Walking stability and sensorimotor function in older people with diabetic peripheral neuropathy. Arch Phys Med Rehabil 2004;85:245-252.

9.Richardson JK, Thies SB, DeMott TK, Ashton-Miller JA. A comprasion of gait characteristics between older women with and without peripheral neuropathy in standard and challenging environments. J Am Geriatr Soc 2004;52:1532-1537.

10. Corriveau H, Prince F, Hébert R, Raiche M, Tessier D, Maheux P, Ardilouze J-L. Evaluation of postural stability in elderly with diabetic neuropathy. Diabetes Care 2000;23:1187–1191.

11.Mueller MJ, Minor SD, Sahrmann SA, Schaaf JA, Strube MJ. Differences in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. Phys Ther 1994;74:299-313.

12.Courtemanche R, Teasdale N, Boucher P, Fleury M, Lajoie Y, Bard C. Gait problems in diabetic neuropathic patients. Arch Phys Med Rehabil 1996;77:849-855.

13. Katoulis EC, Ebdon-Parry M, Lanshammar H, Vileikyte L, Kulkarni J, Boulton AJ. Gait abnormalities in diabetic neuropathy. Diabetes Care 1997;20:1904-1907.

14. Cavanagh PR, Derr JA, Ulbrecht JS, Maser RE, Orchard TJ. Problems with gait and posture in neuropathic patients with insulin-dependent diabetes mellitus. Diabetic Med 1992;9:469-474.

15. Richardson JK, Ching C, Hurvitz EA. The relationship between electromyographically documented peripheral neuropathy and falls. J Am Geriatr Soc 1992;40:1008–1012.

16.Richardson JK. Factors associated with falls in older patients with diffuse polyneuropathy. J Am Geriatr Soc 2002;50:1767-1773.

17. Simoneau GG, Ulbrecht JS, Derr JA.Postural instability in patients with diabetic sensory neuropathy. Diabetes Care. 1994;17:1411-1421.

18. Lafond D, Corrıveau H, Prince F. Postural control mechanisms during quiet standing in patients with diabetic sensory neuropathy. Diabetes Care 2004; 27:173–178.

19. Giacomozzi C, Caselli A, Macellari V,Giurato L, Lardieri L, Uccioli L. Walking strategy in diabetic patients with peripheral neuropathy. Diabetes Care. 2002;25(8): 1451-1457.

20. Giacomozzi C, Ambrogi ED, Macellari LUV. Does the thickening of Achilles tendon and plantar fascia contribute to the alteration of diabetic foot loading?. Clin Biomech 2005;20: 532–539.

21. Nurse MA, Nigg BM. The effect of changes in foot sensation on plantar pressure and muscle activity. Clin Biomech 2001;16:716-727.

22.Caselli A, Pham H, Giurini JM, Armstrong DG,Veves A.The Forefoot-to-Rearfoot Plantar Pressure Ratio Is Increased in Severe Diabetic Neuropathy and Can Predict Foot Ulceration. Diabetes Care 2002;25: 1066-1071.

23. Rao S, Saltzman C, Yack HJ. Ankle ROM and stiffness measured at rest and during gait inindividuals with and without diabetic sensory neuropathy. Gait Posture 2006;24:295-301.

24. Resnick H, Stansberry K, Harris TB, Tiriverdi M, Smith K, Morgan P, Vinik A. Diabetes, peripheral neuropathy, and old age disability. Muscle Nerve 2002;25:43-50.

25. Gutierrez EM, Helber MD, Dealva D, Ashton-Miller JA, Richardson JK. Mild diabetic neuropathy affects ankle motor function. Clin Biomech 2001;16:522-528.

26. Andersen H, Nielsen S, Mogensen CE, Jakobsen J. Muscle strength in Type 2 diabetes. Diabetes 2004;53:1543-1548.

27. Abboud RJ, Rowley DI, Newton RW.Lower limb muscle dysfunction may contribute to foot ulceration in diabetic patients. Clin. Biomech.2000;15:37–45.

28. Kwon OY, Minor SD, Maluf KS, Mueller MJ. Comparison of muscle activity during walking in subjects with and without diabetic neuropathy. Gait Posture 2003;18:105-113.

29. Petrofsky J, Macnider M, Navarro E, Lee Scott. Motor control and gait characteristics in people with type 1 and type 2 diabetes without sensory impairment in the foot. Basic Appl Myol 2005;15(2): 75-86.

30. Andersen H, MogensenPH. Disordered mobility of large joints in association with neuropathy in patients with long-standing insuline-dependent diabetes mellitus. Diabet Med 1997;14:221-227.

31.Eils E, Nolte S, Tewes M, Thorwesten L, Volker K, Rosenbaum D. Modified pressure distribution patterns in walking following reduction of plantar sensation. J Biomech 2002;35:1307–1313.

32.Eils E, Behrens S, Mersa O, Thorwesten L, Völker K, Rosenbaum D. Reduced plantar sensation causes a cautious walking pattern. Gait Posture 2004;20: 54–60.

33.Van den Bosch CG, Gilsing M, Lee S-G, Richardson JK, Ashton-Miller JA: Peripheral neuropathy effect on ankle inversion and eversion detection thresholds. Arch Phys Med Rehabil 1995;76:850-856.

34. Hof AL, Elzinga H, Grimmius W, Halbertsma JPK. Speed dependence of averaged EMG profiles in walking. Gait Posture 2002;16: 78–86.

35. Lelas JL, Merriman GJ, Riley PO, Kerrigan DC. Predicting peak kinematic and kinetic parameters from gait speed. Gait Posture 2003;17:106-112.

36. Otter AR, Geurts ACH, Mulder T, Duysens J. Speed related changes in muscle activity from normal to very slow walking speeds. Gait Posture 2004;19: 270–278.

37. Burnfield JM, Few CD, Mohamed OS, Perry J. The influence of walking speed and footwear on plantar pressures in older adults Clin Biomech 2004;19: 78–84.

38.Segal A, Rohr E, Orendurff M, Shofer J, O'Brien M, Sangeorzan B. The effect of walking speed on peak plantar pressure. Foot Ankle Int. 2004;25(12):926-933.

39.Nymark JR, Balmer SJ, Melis EH, Lemaire ED, Millar S. Electromyographic and kinematic nondisabled gait differences at extremely slow overground and treadmill walking speeds. J Rehabil Res and Dev 2005;42(4):523-534.

40. Van Emmerik REA, McDermott J, Haddad JM, Wegen EEH. Age-related changes in upper body adaptation to walking speed in human locomotion. Gait Posture 2005;22:233-239.

41. England SA, Granata KP. The influence of gait speed on local dynamic stability of walking. Gait Posture 2007;25(2):172-178.

42. Kerrigan DC, Todd MK, Della Croce U, Lipsitz LA, Collins JJ. Biomechanical gait alterations independent of speed in the healthy elderly: evidence for specific limiting impairments. Arch Phys Med Rehabil 1998 Mar;79(3):317-322.

43. Kerrigan DC, Lee LW, Nieto TJ, Markman JD,Collins JJ, Riley PO. Kinetic alterations independent of walking speed in elderly failers. Arch Phys Med Rehabil 2000;81:730-735.

44.DeVita P, HortobagyiT. Age causes a redistribution of joint torques and powers during gait. J Appl Physiol 2000;88: 1804–1811.

45.Graf A, Judge JO, Õunpuu S, Thelen DG. The effect of walking speed on lower-extremity joint powers among elderly adults who exhibit low physical performance. Arch Phys Med Rehabil 2005;86:2177-2183.

46. Van Deursen RWM, Sanchez MM, Derr JA, Becker MB, Ulbrecht JS, R CP. Vibration perception threshold testing in patients with diabetic neuropathy: ceiling effects and reliability. Diabet Med 2001;18:469-475.

47. Hermens HJ, Freriks B, Merletti R, Stegeman D, Blok J, Rau G, Disselhorst-Klug C, Hagg G. Europan Recommendations for Surface Electromyography-Results of the SENIAM Project-Roessening Research and Development b.v.1999.

48. Winter DA. Biomechanics and motor control of human movement. Waterloo, Ontorio:Wiley-Interscience Publication;1990.

7. APPENDICES

7.1.Appendix 1. Ethical Commitee Report

academisch ziekenhuis
Maastricht

P. Debyelaan 25
postbus 5800
6202 AZ Maastricht

telefoon 043-387 65 43
telefax 043-387 78 78

academisch ziekenhuis
Maastricht
azM

Aan: Dr. H.H.C.M. Savelberg
Capaciteitsgroep Bewegingswetenschappen

afdeling MED.ETHISCHE COMMISSIE
uw kenmerk
ons kenmerk MEC 03-041.5
doorkiesnummer 043-38 76009
datum 4 juni 2003

Hierbij bericht ik u dat de Medisch Ethische Commissie op grond van artikel 2.2.a van de WMO op 3 juni 2003 een positief oordeel heeft uitgebracht gelet op het gestelde onder artikel 3 van de WMO met betrekking tot het door u ingediende onderzoeksvoorstel genaamd, "Invloed van spierzwakte op gangbeeld en voetdrukken bij niddm-ers met en zonder polyneuropathie-een cross-sectionel pilot study".

De commissie heeft de volgende stukken in haar toetsing betrokken:
- versie datum protocol 19 maart 2003;
- versie datum deelnemersinformatie 27 mei 2003 en toestemmingsverklaring 19 maart 2003 (inclusief de verzekeringsinformatie over de wijze waarop de verzekering ex artikel 7 lid 1 WMO is geregeld)
- versie datum ABR-formulier 8 mei 2003.

De commissie ontvangt nog graag bericht van de start- en einddatum van genoemde studie.

In een aan deze brief aangehechte bijlage zijn nadere, wettelijke, eisen vermeld waaraan de onderzoeker zal dienen te voldoen of welke door de commissie onder de aandacht worden gebracht.

Met vriendelijke groet,

namens de Medisch Ethische Commissie,

mevrouw mr. dr. W. Kieboom, ambtelijk secretaris

Cc: drs. G.J.H.C.M. Peeters, voorzitter Raad van Bestuur
CCMO

7.2.Appendix 2. Volunteer Information Form

INFORMATIEBRIEF VOOR VRIJWILLIGERS

INVLOED VAN SPIERZWAKTE OP GANGBEELD EN VOETDRUKKEN BIJ NIDDM-ers MET EN ZONDER POLYNEUROPATHIE

Deze informatie is bedoeld om u zo goed mogelijk voor te lichten over het doel van het onderzoek, de wijze waarop het onderzoek wordt uitgevoerd en uw rechten en plichten gedurende het onderzoek. Wij verzoeken u deze informatie zorgvuldig te lezen. Wanneer u daarna nog vragen heeft kunt u deze bespreken met één van de onderzoekers. Op de eerste onderzoeksdag zult u gevraagd worden een schriftelijke verklaring te tekenen waarin u aangeeft dat u deze informatie gelezen heeft en dat u wilt deelnemen.

Doel van dit onderzoek

Ouderdomssuikerziekte gaat vaak gepaard met verminderd functioneren van het zenuwstelsel (polyneuropathie). Het doel van deze studie is om na te gaan in hoeverre achteruitgang van het functioneren van het zenuwstelsel leidt tot verlies van spierkracht en spierfunctie. Een tweede doel is te onderzoeken in hoeverre achteruitgang in spierfunctie drukken onder de voet en bewegingspatronen tijdens lopen en opstaan van een stoel ongunstig beïnvloeden. Deze kennis zal gebruikt worden om trainingsprogramma's te ontwikkelen om achteruitgang in spierfunctie tegen te gaan, en daarmee het functioneren van mensen met ouderdomssuikerziekte in het dagelijkse leven te verbeteren.

Opzet van het onderzoek

Aan dit onderzoek zullen 40 mensen met ouderdomssuikerziekte deelnemen. Een van de complicaties van ouderdomssuikerziekte is dat het functioneren van het zenuwstelsel achteruit kan gaan. Verstoring van de zenuwfunctie kan gevolgen hebben voor het bewegen en daarmee voor de drukken die tijdens lopen of opstaan van een stoel onder de voet ontstaan. In deze studie zullen 20 mensen onderzocht worden die geen last hebben van een verminderde zenuwfunctie, en 20 die daar wel last van hebben. Het onderzoek zal plaats vinden aan de

Universiteit Maastricht, in het bewegingslaboratorium van de capaciteitsgroep Bewegingswetenschappen. Tijdens het onderzoek zal de spierkracht in uw onderbeen gemeten worden, zal uw bewegingspatroon bij twee verschillende loopsnelheden vastgelegd worden en zal bestudeerd worden hoe u van een krukje opstaat. Dit gebeurt in twee verschillende sessies, één sessie voor het bepalen van de spierkracht, één voor het onderzoek naar lopen en opstaan.

Procedure van het onderzoek

Elk van beide onderzoekssessies duurt ongeveer anderhalf uur. Tijdens de eerste onderzoekssessie zal de spierkracht van de kuit- en de scheenbeenspieren gemeten worden. Hiertoe zullen we met behulp van een dynamometer de kracht waarmee u uw voet kunt buigen en strekken meten. Omdat dit afhankelijk is van de hoek van het enkel- en van het kniegewricht zullen we dit doen bij vijf verschillende kniegewrichtshoeken en vijf verschillende enkelgewrichtshoeken. In totaal dus bij 5 x 5 is 25 combinaties van knie- en enkelgewrichtshoeken. Bij elke combinatie zullen we u vragen om enkele seconden lang maximaal eerst uw kuitspieren en vervolgens enkele seconden uw scheenbeenspieren aan te spannen. Na één zo'n meting krijgt u 3 minuten rust, om te voorkomen dat de spieren vermoeid worden. Ankle joints corners.

Om na te gaan of u in staat bent om maximaal uw kuitspieren te activeren, zullen we bij vijf verschillende enkelgewrichtshoeken bij een gestrekte knie, de kuitspier elektrisch stimuleren, terwijl u maximaal kracht uitoefent. Verder zal voor en na de meting door middel van een vingerprik uw bloedsuikergehalte gecontroleerd worden. Tijdens de tweede onderzoekssessie wordt u gevraagd om over een 12 meter lange loopbaan te lopen. In het midden van deze loopbaan bevindt zich een krachtenplatform. Met dit krachtenplatform wordt de kracht die u tijdens het lopen op de grond uitoefent geregistreerd. Tegelijkertijd zullen we ook de activiteit van verschillende beenspieren en de bewegingsuitslagen van het heup-/ knie- en enkelgewricht meten. Dezelfde metingen (gewrichtshoeken, krachten op de vloer en spieractiviteiten) zullen ook uitgevoerd worden terwijl u van een krukje opstaat.

Voordat u begint met lopen, zullen de onderzoekers vier handelingen bij u verrichten. (1) Uw lichaamsgewicht, lichaamslengte en de lengte van het rechterbeen worden gemeten; (2) elektrodes die spieractiviteit meten, worden paarsgewijs op verschillende spieren van uw rechterbeen geplakt; en (3) reflecterende markers die de gewrichtsuitslagen van het heup-/

knie- en enkelgewricht tijdens het lopen meten, worden op anatomische botpunten van uw rechterbeen geplakt. Ook (4) tijdens deze meting zal uw bloedsuikergehalte voor en na de meting bepaald worden.

U loopt met twee verschillende snelheden over de loopbaan: (1) een zelfgekozen, comfortabele snelheid; en (2) een testsnelheid die voor alle vrijwilligers gelijk is. De startpositie op de loopbaan wordt zo gekozen dat u tijdens het lopen met de rechtervoet op het krachtenplatform terechtkomt. Gedurende het lopen is het belangrijk dat u rechtop loopt. Voor de uiteindelijke metingen beginnen kunt u een aantal keren oefenen. De uiteindelijke meting bestaat uit 5 metingen per loopsnelheid. Bij het opstaan van een kruk worden dezelfde metingen uitgevoerd: uw spieractiviteit wordt gemeten, de kracht en de druk onder uw voeten en de bewegingen van de reflecterende markers. Ook bij het opstaan van een krukje zult u gevraagd worden om dit vijf maal te herhalen. Alle metingen die worden verricht zijn gemakkelijk te ondergaan.

Mogelijkheid tot stoppen

Als u besluit deel te nemen aan dit onderzoek staat het u vrij om op ieder moment zonder opgaaf van reden uw toestemming in te trekken en daarmee uw deelname te beëindigen.

Vertrouwelijkheid

Alle persoonlijke informatie zal vertrouwelijk worden behandeld. Uw gegevens zullen alleen beschikbaar zijn voor de onderzoekers. De gegevens die in het kader van het onderzoek verzameld worden, zullen alleen van uw initialen en een codenummer worden voorzien. Uw gegevens worden in computerfiles opgeslagen. Indien gewenst kunt u inzicht krijgen in uw eigen gegevens en zal worden uitgelegd wat het een en ander betekent.

Medisch Ethische Commissie

De Medisch Ethische Commissie van het Academisch Ziekenhuis Maastricht/ Universiteit Maastricht heeft een positief oordeel gegeven m.b.t. dit onderzoek. U heeft recht op inzage in of een kopie van de brief waarin zij een positief advies geven m.b.t. deze studie.

Verzekering

Alle deelnemers aan het onderzoek zijn door de Universiteit Maastricht verzekerd in verband met eventuele schade die hij/zij mocht lijden als gevolg van deelnamen aan dit onderzoek, conform de eisen van de wet WMO (Wet Medisch Wetenschappelijk Onderzoek met mensen).

Vergoeding

Als compensatie voor uw deelname aan het volledige onderzoek, ontvangt u een financiële vergoeding van 25 Euro. Daarnaast is er een tegemoetkoming in de reiskosten beschikbaar. De vergoeding wordt overgemaakt naar uw bank- of girorekening aan het einde van uw deelname.

Contactpersonen

Wanneer u na het lezen van deze informatie vragen heeft of meer informatie wilt ontvangen, kunt u bij de onderzoekers Martine Bakker, Marloes van Riemsdijk of Ellen Sesink terecht of kunt u contact opnemen met onderzoekscoördinator Dr. H. Savelberg of Dr. K. Meijer. Daarnaast bestaat de mogelijkheid om een onafhankelijk, en niet bij het onderzoek betrokken, arts te raadplegen.

Onderzoeksteam

Dr. Hans Savelberg, onderzoekscoördinator, tel werk: 043-3881392,
Faculteit der Gezondheidswetenschappen, Cap.groep, Bewegingswetenschappen
Dr. Kenneth Meijer, onderzoekscoördinator, tel werk: 043-3881384
Faculteit der Gezondheidswetenschappen, Cap.groep Bewegingswetenschappen
Drs. Ellen Sesink, onderzoeker, tel werk: 043-3881394
Faculteit der Gezondheidswetenschappen, Cap.groep Bewegingswetenschappen
Martine Bakker, Marloes van Riemsdijk, stagiaire onderzoekers
Studenten Universiteit Maastricht, Faculteit der Gezondheidswetenschappen, Capaciteitsgroep Bewegingswetenschappen
Onafhankelijke arts

Met vragen over het onderzoek kunt u zich eventueel ook wenden tot een arts die niet betrokken is bij het onderzoek:

Dr. Hans Keizer

Tel werk: 043-3881397
Adres:Faculteit der Gezondheidswetenschappen, Vakgroep Bewegingswetenschappen
Universiteitssingel 50, 6229 ER Maastricht
Bewegingslaboratorium, ruimte 2.249, tel. bewegingslaboratorium: 043-3881391

7.3. Appendix 3. Patient Confirmation Letter

TOESTEMMINGSVERKLARING

Verklaring deelname aan het onderzoek: **INVLOED VAN SPIERZWAKTE OP GANGBEELD EN VOETDRUKKEN BIJ NIDDM-ers MET EN ZONDER POLYNEUROPATHIE**

Hierbij verklaar ik kennis genomen te hebben van de informatie over het onderzoek. Op basis van deze informatie heb ik besloten om deel te nemen aan dit onderzoek.

Ik ben ervan op de hoogte dat ik op elk moment verdere medewerking aan het onderzoek kan weigeren.

Gegevens proefpersoon:

Naam en voornaam:……

Adres:.....…….

Postcode en woonplaats:…….....……

Telefoonnummer:…….....……...

Bank /Giro rekeningnummer:……

Sofi-nummer:……..

Plaats:……. Datum:……

Handtekening proefpersoon:……..