

The combined effect of heat and vitamins on gait and balance in people with mobility impairments

By Jerrold Petrofsky Ph DMichael Laymon D ScIman Khowailed D Sc

Dept. of Physical Therapy, Touro University, Henderson Nevada

Jerrold Petrofsky, 931 American Pacific Drive #107, Henderson, Nevada 89014

Abstract:- Purpose- To determine if the use of heat and heat plus vitamins can increase mobility and balance stability in people with mobility impairments. **Problem-** Mobility loss is a major concern in the older population. It is a leading cause of falls and death. A previous study showed that heat helps mobility and balance. Antioxidants plus heat may even reduce cellular inflammation.

Subjects- Eighty healthy subjects free of any headaches, diabetes mellitus, and orthopedic or neurological conditions beyond normal aging were recruited. Subjects were sedentary individuals that were not participating in any balance or walking exercises regularly. Subjects were instructed not to take any medication or central nervous stimulants that might affect their balance the day before and during the study. The age range was 25-64 years old. Twenty were controls and had no heat, 20 had heat only, 20 vitamins plus heat, and 20 vitamins only. The experimental protocol was approved by the Solutions Institutional Review Board and all protocols and procedures were explained to each subject and the subjects gave their written informed consent for the study.

Intervention- Subjects received nothing (controls) or vitamins, or heat, or vitamins and heat. Heat was provided with ThermoCare heat wraps over a 2-week period. Vitamins were used for a 4-month period.

Outcome measures-

1. Modified Oswestry test for lower back disability. It includes 10 sections of questions related to pain and disability and is used by disability examiners.
2. Analogue visual scale for mobility
3. Balance tests
4. Time up and go tests
5. Walking test
6. Treadmill EMG and impact ground reaction forces

I. Rationale-

ThermoCare heat wraps, in a previous study, have been shown to increase mobility and improve balance. In previous studies, vitamins have been shown to increase mobility. This study will look at the 2 arms independently and together to see if a combination of vitamins and heat can help mobility and balance even more.

II. Results-

Vitamins for 4 months or heat alone increased mobility. This is evidenced by better balance, less muscle tremor and faster and more stable gait, especially with the 2 used together. The fact that the controls showed no change in balance or gait over 4 months shows the lack of a training effect of the procedures and makes the effects seen on balance and mobility by vitamins and heat more significant. Heat alone significantly increased balance and mobility. Vitamins alone also accomplished this. The 2 used together were synergistic yielding better mobility than either alone. In the one group where bone density was measured, there was a significant increase in bone density over the 4-month period showing a reversal in the progression to osteoporosis.

III. CONCLUSIONS-

Using vitamins alone for 4 months produced significantly less sway and decreased tremor on balance testing. Interestingly, even 2 months on vitamins produced a significant reduction in tremor and sway. Thus vitamins alone improved balance. After 4 months on vitamins, subjects reported better mobility as assessed by increased speed of gait and faster stand up times from sitting.

1. Heat alone also increased balance and mobility after 10 days of use.
2. Heat and vitamins were synergistic producing even better improvements in balance and mobility than heat or vitamins alone.

3. In one group, where bone density was measured, there was a significant increase in bone density following 4 months of taking Caltrate and vitamin D.
4. Compliance for taking the vitamins and using heat were very good.
5. Risk to develop osteoporosis was reduced with 4 months on this regime.

IV. INTRODUCTION

Mobility and the elderly- It is well established that gait and balance impairments are common in the elderly. Due to the shift in the population toward an older average age, this problem becomes important to address. The most significant problem is not the loss of mobility itself, but falls associated with poor balance. These can cause, in a population with osteoporosis, deadly falls. Falls are one of the most prevalent causes of injury and death in the elderly population[1]. One in every three adults ages 65 and older falls each year [2]. In 2010, 2.4 million non-fatal fall injuries in older adults were treated in emergency rooms and over 22,000 older adults died from unintentional fall injuries[3]. The length of hospital stay is about twice that of a younger person after a fall[4]. Falls reduce the quality of life by reducing confidence and independence[5] even if people don't fall since it is a fear that they must live with [6]. The elderly can present with greater postural sway, which is strongly associated with a greater risk of falling[7]. Between 30 and 50% of the elderly will fall annually and in people 65 and older and 50% of those fall routinely [1, 5]. About 5% of the falls result in fracture and is the 6th leading cause of death in the elderly[8]. Poor balance places the elderly at risk for falls during gait as well. Some of the contributing factors are muscle strength deficits[9], lack of good muscle control and loss of coordination[10], impairments in vision and the vestibular system[11], and lack of proprioception in the joints and feet[12]. Thus, many body systems are altered by ageing and can contribute to poor gait stability and falls. The lack of muscle control or muscle weakness (sarcopenia) and stiffness in joints causes the elderly to adopt a slower gait and wider stance to avoid falls [13, 14]. Loss of cognitive thinking ability can also lead to poor gait and increased risk of falls [15]. A Cochrane review of falls in the elderly identified the importance of attacking multiple factors in reducing falls and not just one item[16].

Role of heat- Of these multiple impairments, heat may have a positive benefit on several of them. Heat increases conduction velocity of nerves and increases the speed of reflexes[17]. It also increases flexibility of ligaments and tendons and other soft tissue[18-22]. Heat also increases circulation[17, 23-28]. Impaired circulation may also reduce nerve conduction velocity and reduce motor function. Finally heat has been shown to reduce pain[29], allowing gait to improve as well as balance. But one of the positive benefits of heat is increased healing in tissue through an increase in tissue metabolism and blood flow[30, 31]. But part of healing is also reducing tissue inflammation. Heat acutely increases swelling and inflammation but chronically increases healing. An additional benefit may be seen if heat is added to ingestion of antioxidants. This would protect tissue from the oxidative radicals released with higher tissue temperatures and should promote healing[32, 33]. Several antioxidants have shown such potential in increasing mobility.

Vitamin D-

Vitamin D deficiencies have been associated with poor mobility and arthritis [34-37]. One of the contributing mechanisms is loss in muscle strength (sarcopenia) which is inversely related to vitamin D in the elderly[38]. While some studies show little effect on falls, a recent review of 8 studies with a meta-analysis showed that falls were reduced when vitamin D was ingested at 800 IU per day [39-44]. Sarcopenia is a well known symptom (proximal) of vitamin D deficiency [45, 46]. There are vitamin D receptors in skeletal muscle that cause muscle to build strength [47-49]. A primary role of vitamin D is in down regulating inflammation. Concentration of TNF alpha and other inflammatory cytokines is reduced with higher serum levels of vitamin D[50]. Obesity is inversely related to vitamin D serum levels as is general inflammation[51]. Adipose tissue secretes more than 200 tissue cytokines. These are down regulated by vitamin D[52-54]. In some populations such as Asians, vitamin D ingestion reduces tissue inflammation and the inflammatory response to stress. It also increases the blood flow response to stress [55].

Coenzyme Q10-

Coenzyme q10 is an enzyme linked to energy production in the mitochondria. It has been shown for years that it increases cellular ATP when administered orally[56]. Supplementation with Co-Q10 has been shown to increase the blood flow response to stress and reduce inflammation [57]. After administration of vitamins (1000 mg of vitamin C, 800 IU of vitamin E, and 300 mg of Coenzyme Q-10) for 14 days, skin blood flow to vascular occlusion and local heat following a high fat meal significantly decreased and free radicals significantly increased at 2 hours compared to baseline. When vitamins were given, the blood flow response to vascular occlusion and local heat before and after high fat meals were not significantly different [32, 33, 58].

Vitamin E-

Vitamin E is a well-known antioxidant[59]. It reduces tissue inflammation and increases blood flow in response to stress[32, 33]. Its use is associated with reduced oxidative stress and tissue healing[60]. Antioxidants like vitamin E have been shown to slow the age associated oxidative process[61].

Subjects

Eighty healthy subjects free of any headaches, diabetes mellitus, and orthopedic or neurological conditions beyond normal aging were recruited. Subjects were sedentary individuals that were not participating in any balance exercises regularly. The age range was 25-64 years old. Twenty were controls and had no heat, 20 had heat, 20 vitamins plus heat, and 20 vitamins only. The general characteristics are given in Table 1. The experimental protocol was approved by the Solutions Institutional Review Board and all protocols and procedures were explained to each subject and the subjects were give their written informed consent for the study.

Table 1. General characteristic of subjects Control group (n=20)

Characteristic	Mean (SD)	n (%)
Age (years)	60.1 (8.9)	
Gender (Female)		56
Weight (Kg)	89.8 (12.5)	
Height (Cm)	163.5 (10.9)	

Abbreviations: SD, standard deviation; BMI, Body Mass Index Heat only group (n=20)

Characteristic	Mean (SD)	n (%)
Age (years)	58.1 (8.3)	
Gender (Female)		61
Weight (Kg)	85.3 (6.4)	
Height (Cm)	164.7 (10.6)	

Abbreviations: SD, standard deviation; BMI, Body Mass Index Vitamin only group (n=20)

Characteristic	Mean (SD)	n (%)
Age (years)	58.3 (10.2)	
Gender (Female)		55
Weight (Kg)	93.8 (9.3)	
Height (Cm)	165.0 (6.1)	

Abbreviations: SD, standard deviation; BMI, Body Mass Index Heat plus vitamin group (n=20)

Characteristic	Mean (SD)	n (%)
Age (years)	60.9 (8.9)	
Gender (Female)		51
Weight (Kg)	90.7 (9.5)	
Height (Cm)	165.8 (10.9)	

Abbreviations: SD, standard deviation; BMI, Body Mass Index

V. METHODS

Fall questionnaire

A fall questionnaire was used to screen the subjects. It was developed and validated in other studies [62]. A score of greater than or equal to 4 was considered as an indicator of high risk for falls. Analog Visual Scale for Perceived Gait Exertion The visual analog gait ability scale that was used in this study was from 0 to 10. Subjects placed a vertical mark across a 10 cm horizontal line such that the closer they mark the mark to the 10 cm point, the greater was their difficulty in gait. The first step in calculating the combined difficulty was to multiply the visual analog score by 10. Thus, the score went from 0 to 100. One hundred on this scale was extremely hard mobility whereas zero was no impairment. Balance testing- Measurement of postural sway to

assess postural stability, a force platform was used. The displacement of the center of pressure (COP), mean COP positions, length of the COP path, sway velocity, area of COP path and root mean square area have been used to determine the postural sway. Some studies used coefficient of variation (CV) of the weight displacement as measures of the postural sway [63, 64]. In this study, CV of the polar vector of weight displacement was used as the measurement of postural sway. Also, tremor was assessed in the 8 Hz band of the variation of movement on the platform. The validity and reliability of this force platform has been established in a previous study [65]. Eight quiet standing balance tasks were conducted in this study. Sensory variables such as the vision, base of support and surface compliance were altered individually or simultaneously in the balance tasks. To alter the visual input, two levels of vision (eyes open and closed) were used in the balance tasks. To alter the somatosensory input, two different surface compliances (firm surface and foam) were used (Table 2). Subjects were asked to stand in two different stance positions with feet apart or in tandem (feet in a heel-toe position with non-dominant foot in front)[66].

The balance platform was 1 m by 1 m in size and 0.1 m in height. The validity and reliability of this force platform has been established in a previous study [65]. Four stainless steel bars, each with four strain gauges, are mounted at the four corners under the platform (TML Strain Gauge FLA-6, 350-17, Tokyo, Japan). The output of the 4 Wheatstone strain gauge bridges is amplified by a Biopac MP35 low-level bio-potential amplifiers and digitized through a 24-bit A/D converter. The sampling rate is 1000 samples per second [65]. To calculate the load and the center of the pressure of the force on the platform, the output of the four sensors is used to measure the X and Y coordinates of the center of gravity of the subject. This data is converted to a movement vector giving a magnitude and angular displacement. By averaging this movement vector over 6 seconds, mean and standard deviation (SD) will be obtained for this measure. From this, the Coefficient of Variation (CV) of the polar coordinate was calculated ($SD \div \text{Mean} \times 100\%$) as a measure of the postural sway [65]. The average CV of each task is determined over a 5 second sample of the data.

Table 2. Eight balance tasks in the study

Station	Position	Number of altered factor	Sensory Factor(s)
TEO-FIRM	<i>Tandem standing</i>	1	Base of support
	Eyes open		
	Firm surface		
FAEO-FOAM	Feet apart	1	Surface compliance
	Eyes open		
	<i>Foam surface</i>		
FAEC-FIRM	Feet apart	1	Vision
	<i>Eyes closed</i>		
	Firm surface		
TEO-FOAM	<i>Tandem standing</i>	2	Base of support
	Eyes open		Surface compliance
	<i>Foam surface</i>		
TEC-FIRM	<i>Tandem standing</i>	2	Base of support
	<i>Eyes closed</i>		Vision
	Firm surface		
FAEC-FOAM	Feet apart	2	Vision
	<i>Eyes closed</i>		Surface compliance
	<i>Foam surface</i>		
TEC-FOAM	<i>Tandem standing</i>	3	Base of support
	<i>Eyes closed</i>		Vision
	<i>Foam surface</i>		Surface compliance

Gait testing

Treadmill testing on Noraxon pressure system-Gait testing was accomplished in two ways. Subjects stood for 30 seconds to obtain static pressure measures under the feet. Next subjects walked on a treadmill at 2.5 mph at 0% grade. The treadmill (Noraxon Inc. Scottsdale Az.) has pressure sensors under the belt to measure temporal gait parameters and ground reaction forces. Two infrared cameras captured motion of the body (myovideo high speed analysis system). Sensors were placed on the hip, knee and ankle and foot to capture motion. Finally, electromyography (EMG) was recorded via a telemetry system as part of the treadmill for the medial and lateral quadriceps, hamstring, gastrocnemius and tibialis anterior muscles. A picture of the system is shown in Figure 1. Treadmills produce different gait than that seen during normal walking since the belt is moving under power. For normal gait, the Protokinetics Zeno walkway which provided timing and pressure was used. The treadmill forces gait speed by its nature of a motor moving the belt. The Zeno walkway allowed subjects to walk at a comfortable speed for the TUG test and walking tests. The faster a person can stand up and walk, the less chance of falling [67, 68]. The TUG started with the subject sitting in a chair and on visual command would stand up and walk 3 meters. This was repeated two times. The second walking test involved walking 13 meters on the walkway at a self-paced speed (Figure 2,3).



Figure 1- Noraxon pressure mat treadmill used for impact forces and muscle activity.

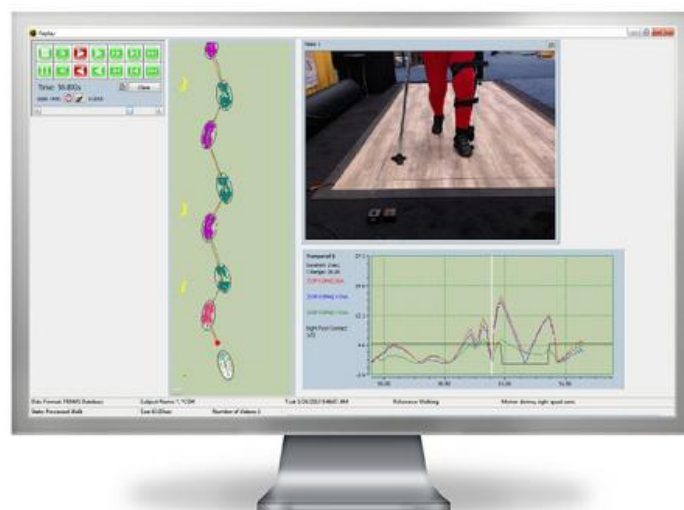


Figure 2- the Protokinetics walkway.

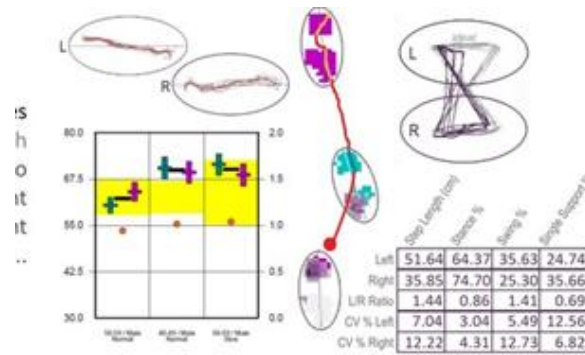


Figure 3- Pressure analysis during gait on the Protokinetics walkway.

NIH standard mobility testing- Two tests were used for mobility as specified by the National Institutes of Health. These were the Timed Up and Go (TUG) and walking tests. The TUG starts with the subject sitting in a chair and on visual command will stand up and walk 3 meters, turn 180 degrees, walk back 3 meters and return to sitting. This was repeated two times. The second walking test involved walking 40 feet on the walkway at a self-paced speed. Temporal and pressure characteristics will be recorded under the two test conditions. Home heat use compliance score- Subjects kept a home heat compliance log. They scored for each day they were to participate and used LLCH wrap as a percentage score for how much they left the heat on. For example, if they used it for 3 hours and were to use it for 4 hours, they scored 75%. Home vitamin compliance score- Subjects keep a home vitamin compliance log. They scored for each day they are to participate. Bone density- In one group of 20 subjects, bone density was measured at the beginning and after 4 months of taking vitamins. This was a pilot to see if there would be a difference. Bone density was measured at the calcaneus by ultrasound. The unit was calibrated against standards each day just before the measurements were made. The unit was Sahara, by Hologic, Inc. 35 Crosby Drive, Bedford, MA.

Application of heat- Heat was applied with a dry heat wrap (ThermaCare, Pfizer Consumer Healthcare, Richmond, VA). The warm wrap kept the average skin temperature at about 42 degrees C and was applied as per manufacturer’s instructions around the lower back. It was kept on for 4 hours.

Vitamins- Each day in the vitamin groups subjects took the following;4000 units vitamin D1000 units vitamin E300mg CoQ101 tablet Caltrate1 multivitamin.

Procedures

This was a controlled cross sectional study lasting 4 months in duration. Subjects first entered the laboratory and filled out the IRB documentation and rested for 15 minutes. Medical screening of subjects was conducted and appropriateness for inclusion determined. Next, balance was tested on the balance platform. Gait was then analyzed during the NIH TUG and walking tests. The analogue visual gait difficulty scale was filled out to see daily perceived exertion levels during gait. Subjects were then tested as described under methods for static balance and walking on the Noraxon treadmill. These measures were completed at day 0 and at 2 months, and 4 months. Subjects were evaluated and came to the laboratory at 1 month and 3 months to assure compliance with the program. If heat was applied, it was used daily for the last 2 weeks of the study. There were 4 groups of subjects, 20 in each group for a total of 80 subjects. One group was the control group, one a heat group, one a heat plus vitamins and one a vitamin only group.

VI. RESULTS

Control Group-Balance-

The results of the measurements of balance on the balance platform is shown in Figures 4 and 5The tests are in increasing order of complexity such that the easiest test is near the left of the x axis and the hardest is on the right side of the graph.

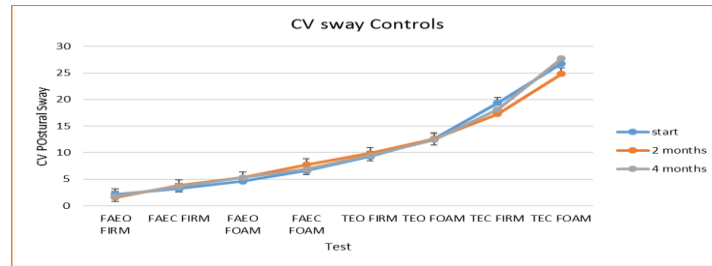


Figure 4- The coefficient of variation of postural sway during 8 balance tasks in all of the subjects under 3 conditions; start, after 2 months and after 4 months.

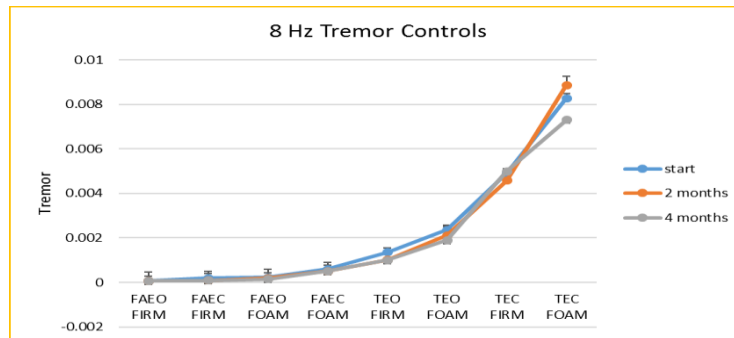
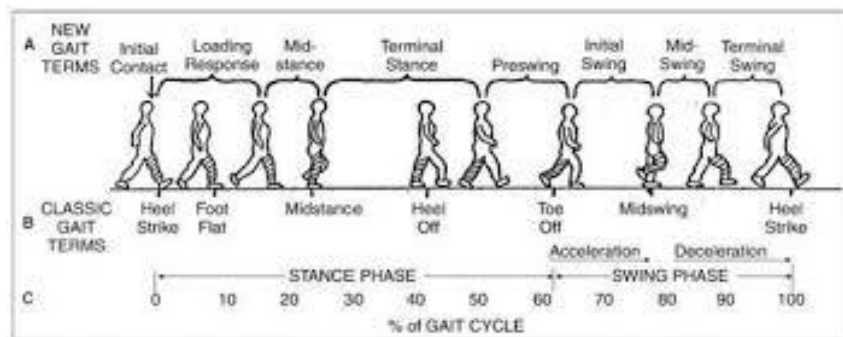


Figure 5- The tremor during the 8 balance tasks in all subjects at 3 times; start, after 2 months and after 4 months.

For the control group, when one factor was altered, comparing feet apart eyes open on foam compared to a firm base of support, there was a 3-fold increase in postural sway. When 2 factors were altered (feet apart eyes closed foam) compared to feet apart eyes open firm, the control group showed a 12-fold increase whereas after intervention, a similar comparison showed almost a 5-fold increase in sway ($p < .001$). Finally, with 3 factors altered, with eyes closed, tandem standing on foam, the sway in the group under control condition increased, compared to the easiest task, sway increased about 20 fold ($p < .001$). (Figure 4) There was no significant difference at the start, 2 months or 4 months in the sway data for any one test in the control group (ANOVA $p > 0.05$). In the 6-10 Hz bandwidth, tremor increased significantly in the control group for the 4 most difficult balance tasks ($p < .01$) (Figure 5). There was no significant difference at the start, 2 months or 4 months in the tremor data for any one test in the control group (ANOVA $p > 0.05$). Treadmill Data-Muscle activity controlling the knee was assessed by measuring the electromyogram (EMG) at 2 heads of the quadriceps, the vastis medialis and lateralis. More EMG activity signifies more control of the knee. The loading response is best shown in Figure 6 showing the phases of the gait cycle.



1. Figure 6- A diagram of the gait cycle showing the time when the foot hits the ground. As it hits, the force that comes from ground contact on initial contact is called the ground reaction force while the loading response is from initial contact through mid and late stance.

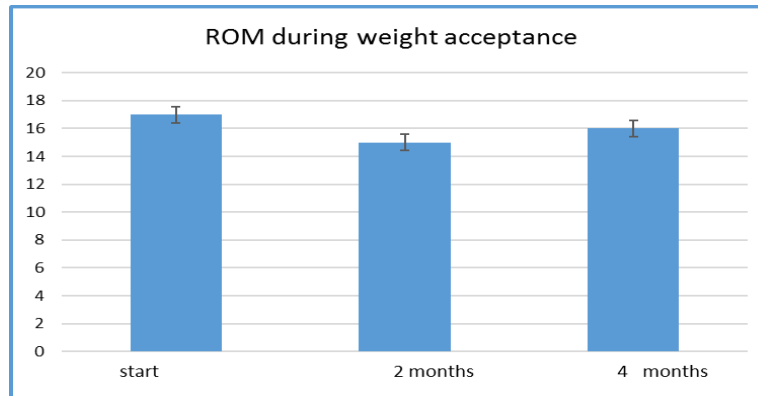


Figure 7- Change in range of motion during gait on the treadmill in control subjects.

As shown in Figure 7, there was no change in range of motion at the knee during the weight acceptance phase of gait comparing the initial, middle and 4 month measures (ANOVA $p>0.05$).

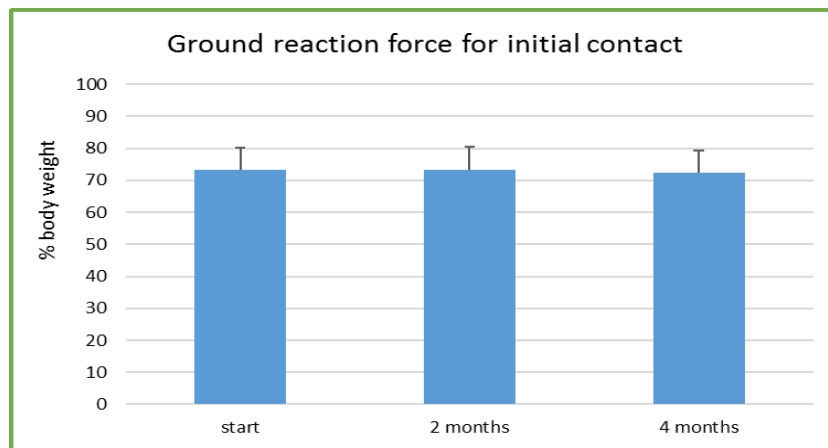


Figure 8- The ground reaction force of the foot on initial contact at the start, after 2 months and after 4 months in the control group.

As shown in Figure 8, there was no change in the ground reaction force in the control subjects over the 4-month period ($p>0.05$).

Likewise, as shown in Figure 9, there was no change in EMG comparing start, 2 months and 4-month data ($p>0.05$).

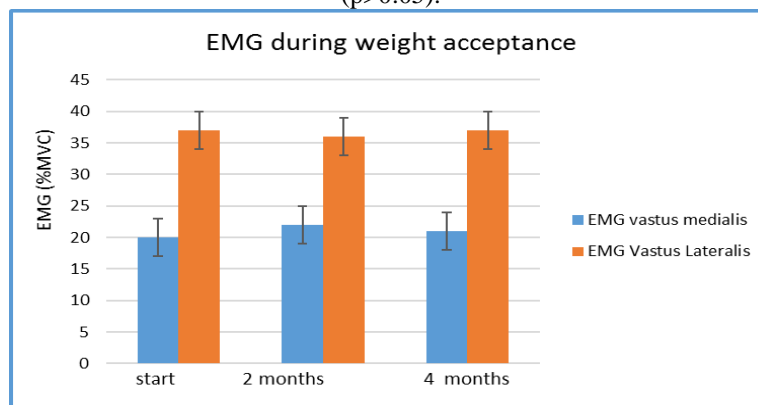


Figure 9- The muscle activity of the knee extensors on the medial and lateral knee in the control subjects at the start, after 2 months and after 4 months.

	Spatial Parameters			Temporal Parameter		
	Step Length	Stride length	Step Width	Step Time	Stride Time	Cadence
start	52.6	107.0	12.8	0.6	1.3	98.6
SD	4.7	8.5	3.4	0.1	0.1	8.2
2 months	52.1	106.0	12.7	0.6	1.2	97.7
SD	4.7	8.5	3.4	0.1	0.1	8.1
4 months	52.8	107.5	12.9	0.6	1.3	99.1
SD	4.8	8.6	3.4	0.1	0.1	8.2

Table 3- temporal and spatial gait on the treadmill in the control group

There was no difference in knee extensor activity during the 4 months of measurements. There was no change in temporal or spatial gait timing on the treadmill as well as shown in Table 3.

Zeno walkway-Gait speed-The speed of gait in the control group is shown in Figure 10. There was no difference from the start, to the middle, to the end of the study ($p>0.05$ ANOVA).

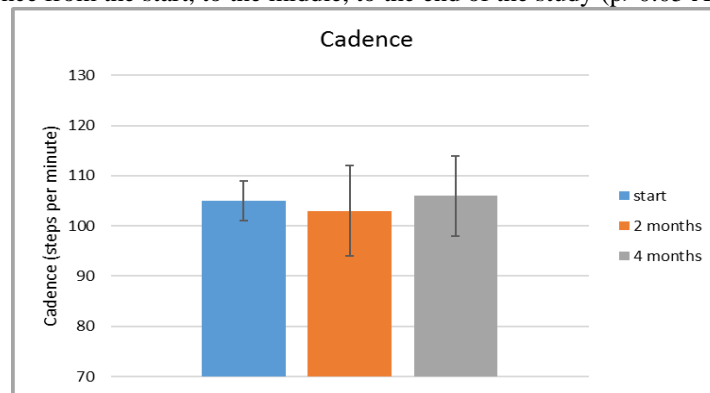


Figure 10- The gait speed in the subjects after no heat at the beginning, after 2 months and after 4 months in the control group. Data is the mean +/- the standard deviation of the group.

Gait symmetry- Gait symmetry is the key to preventing falling. Asymmetric gait can lead to falls. It was measured in 2 ways, the coefficient of variation of side to side movement of the body in the stance phase and in the swing phase.

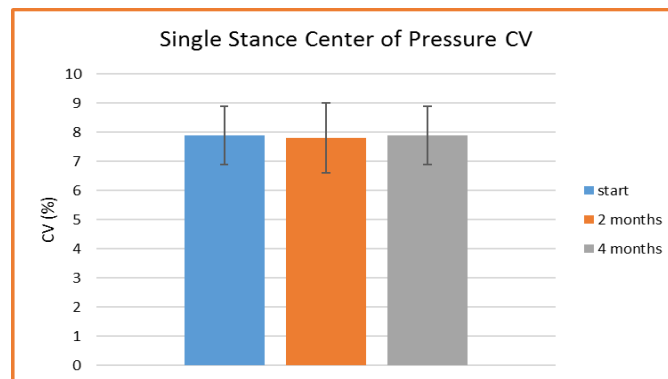


Figure 11- The gait symmetry in the subjects in the control subjects at the beginning and after 2 and 4 months. Data is the mean +/- the standard deviation of the group for the single stance phase.

Coefficient of variation of weight shift during gait

The coefficient of variation in weight shift during steps is shown in Figures 11 and 12. This is important because it quantifies a measure of side to side sway during walking. The greater the side to side sway, the greater the chance of falling [69-71]. The measure is called the coefficient of variation of the center of pressure. The single stance variation in center of pressure during gait was not different in the control group comparing the 3 measuring periods (ANOVA $p>0.05$). For the double stance portion of the gait cycle, a similar result was seen as shown in Figure 12.

Angle of the foot-The angle of the foot during gait is shown in Figure 13.

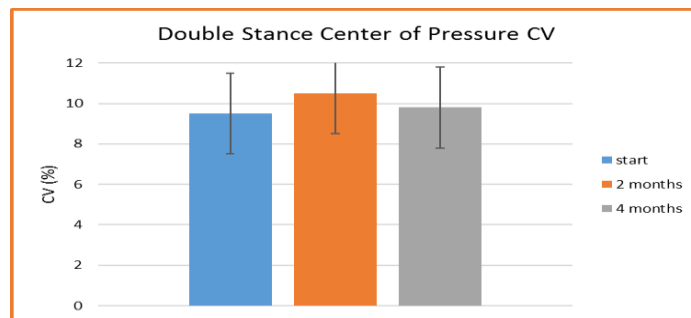


Figure 12- The gait variation in the control subjects at the beginning, after 2 months and after 4 months. Data is the mean +/- the standard deviation of the group for the double stance phase.

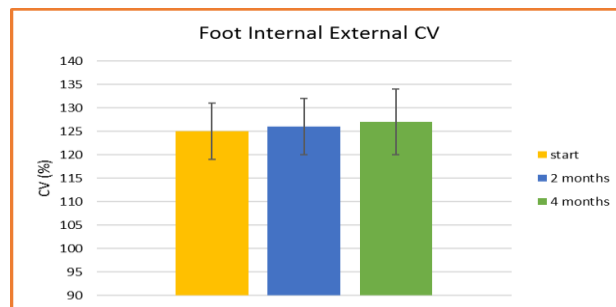


Figure 13- The cadence external rotation of subjects at the start, after 2 months and after 4 months in the control group. Data is the mean +/- the standard deviation of the group.

Internal-external rotation whose coefficient of variation was over 100%, was not different at the 3 measuring periods in the control subjects.

Heat Only Group-

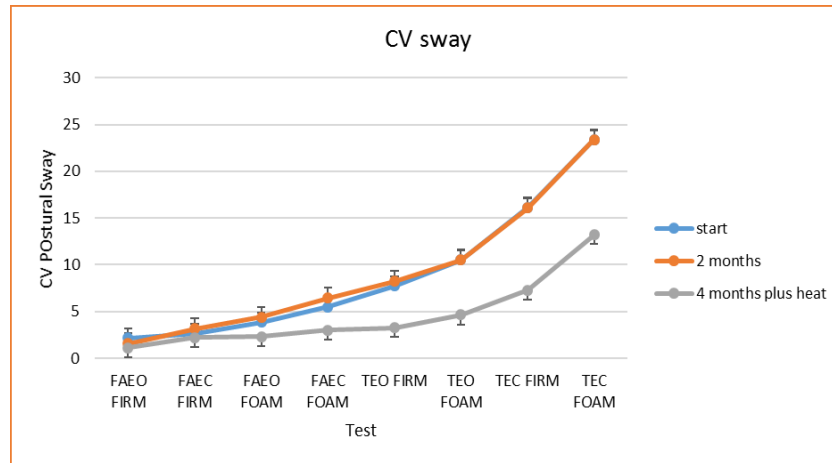


Figure 14- The coefficient of variation of postural sway during 8 balance tasks in all of the subjects under 3 conditions; start, after 2 months and after 4 months in subjects using heat.

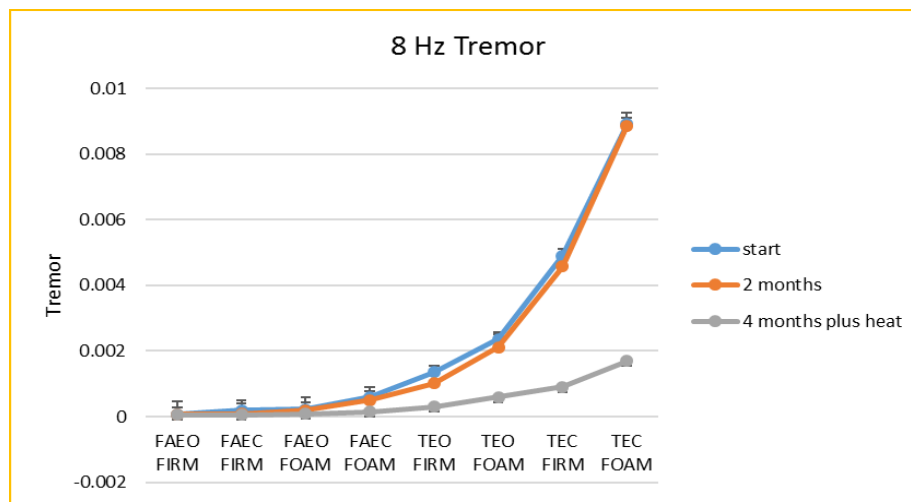


Figure 15- The tremor during the 8 balance tasks in all subjects at 3 times; start, after 2 months and after 4 months in subjects using heat.

For the heat group, when one factor was altered, comparing feet apart eyes open on foam compared to a firm base of support, there was a 3-fold increase in postural sway which was the same as the control group at the 2-month point. This is not surprising since there was no intervention. Heat was only applied the last 2 weeks where a significant reduction in sway was seen in the 4 most difficult balance tasks ($p < 0.01$) (Figure 14). In the 6-10 Hz bandwidth, tremor increased significantly in the heat group for the 4 most difficult balance tasks ($p < .01$) (Figure 15) but was reduced significantly on the last measurement period after heat was applied ($p < 0.05$).

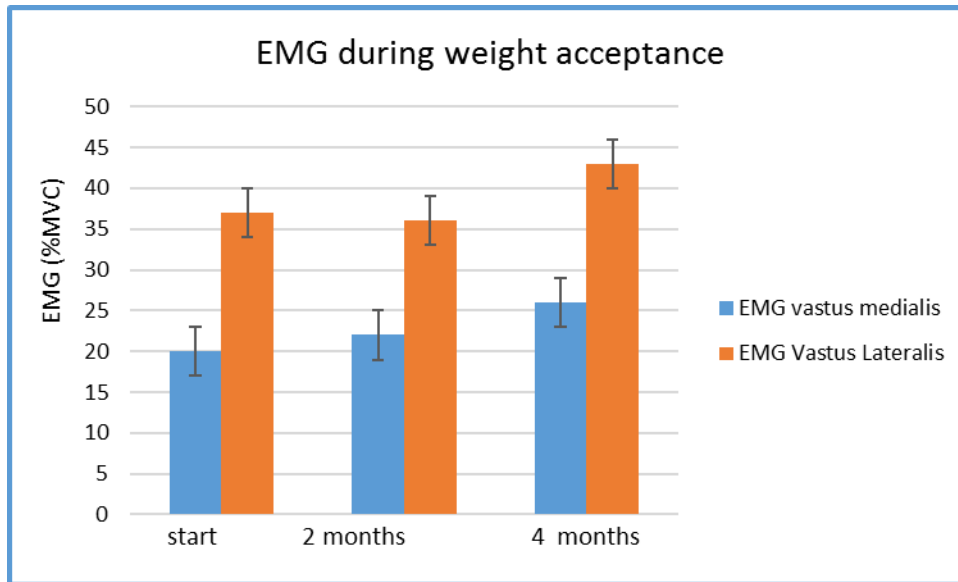


Figure 16- The muscle activity of the knee extensors on the medial and lateral knee in the control subjects at the start, after 2 months and after 4 months.

The EMG of the vastus medialis and lateralis was not different in the first 2 months. But after heat was applied, EMG activity increased significantly in both muscle groups compared to the control or 2-month data ($p < 0.01$).

	Spatial Parameters			Temporal Parameter		
	Step Length	Stride length	Step Width	Step Time	Stride Time	Cadence
start	54.3	107.4	12.9	0.6	1.3	97.3
SD	4.4	8.6	3.2	0.0	0.1	7.8
2 months	54.6	106.9	12.9	0.6	1.3	98.1
SD	3.8	7.1	3.1	0.0	0.1	7.1
4 months	51.2	102.8	11.1	0.5	1.0	105.4
SD	4.0	7.1	3.8	0.0	0.1	9.2

Table 4- temporal and spatial characteristics of gait in the heat group.

As shown in Table 4, the gait increased in speed in the last month after heat was applied for the last 2 weeks.

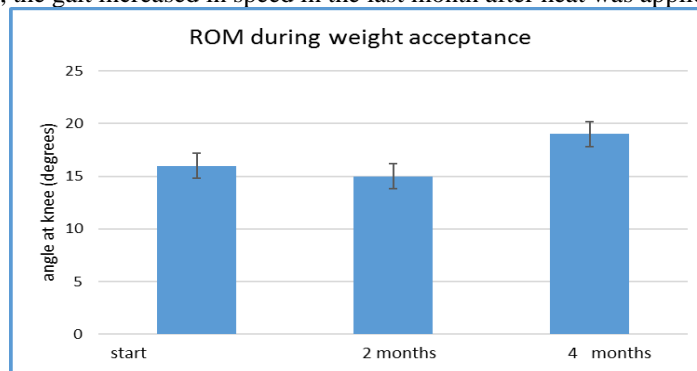


Figure 17- Change in range of motion during gait on the treadmill in heat subjects.

As shown in Figure 17, there was no significant difference in the range of motion at the knee during the weight acceptance phase of gait when comparing the data from the start and the 2-month measurement. But, after heat

was applied, there was a significant increase in the range of motion at the knee during this phase compared to the start and 2-month data ($p < 0.01$).

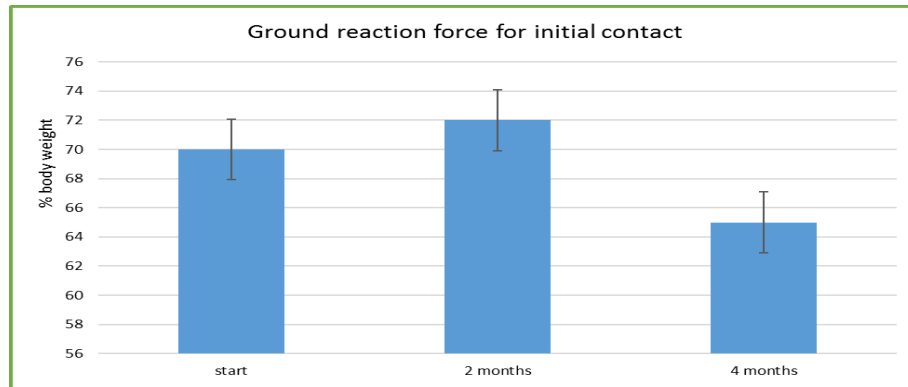


Figure 18- The ground reaction force of the foot on initial contact at the start, after 2 months and after 4 months in the heat group.

As was the case in Figure 18, the ground reaction forces were reduced after heat was applied and were significantly lower than the start and 2-month data ($p < 0.01$) which were not different from each other ($p > 0.05$).

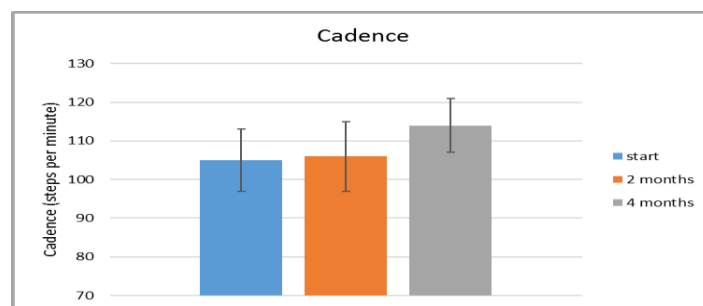


Figure 19- The gait speed in the subjects after no heat at the beginning, after 2 months and after 4 months in the heat group. Data is the mean +/- the standard deviation of the group.

As shown in Figure 19, the cadence, which was no significantly different when comparing start data to month 2 ($p > 0.05$), was significantly higher after heat was applied ($p < 0.01$) compared to the start and 2 month results.

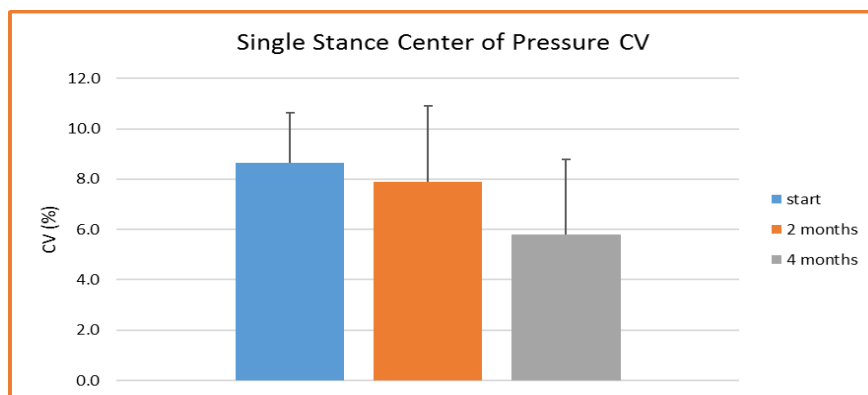


Figure 20- The gait symmetry in the subjects in the heat only subjects at the beginning and after 2 and 4 months. Data is the mean +/- the standard deviation of the group for the single stance phase.

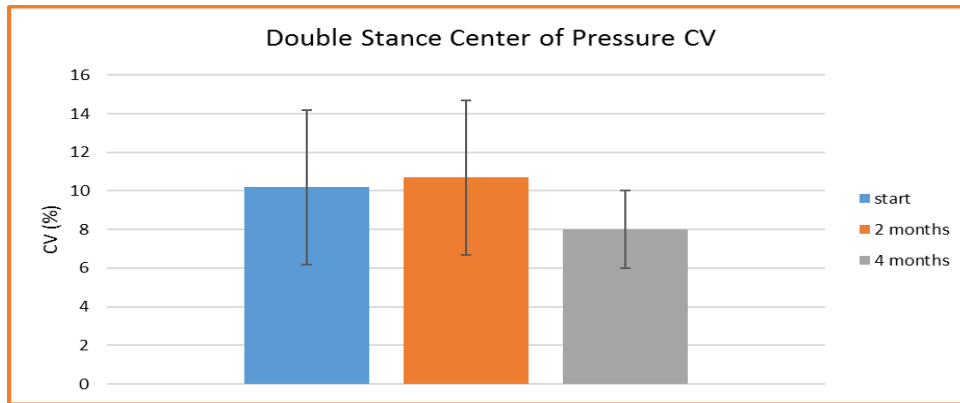


Figure 21- The gait variation in the heat subjects at the beginning, after 2 months and after 4 months. Data is the mean +/- the standard deviation of the group for the double stance phase of the heat group.

The single and double stance center of pressure (Figures 20 and 21) was not different between the start and 2-month data but was significantly less after heat was used compared to the other 2 measuring periods ($p < 0.01$).

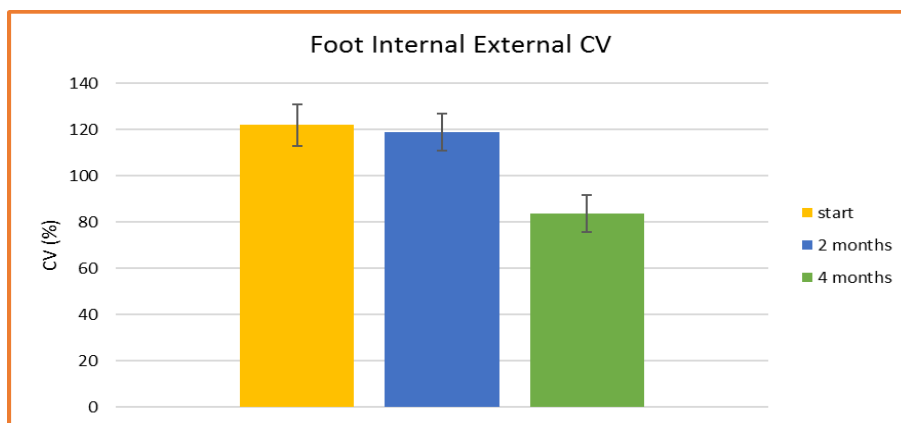


Figure 22- The cadence external rotation of subjects at the start, after 2 months and after 4 months in the heat group. Data is the mean +/- the standard deviation of the heat group.

Finally, the internal external rotation of the foot during gait was significantly less when heat was used as well showing steadier gait (Figure 22).

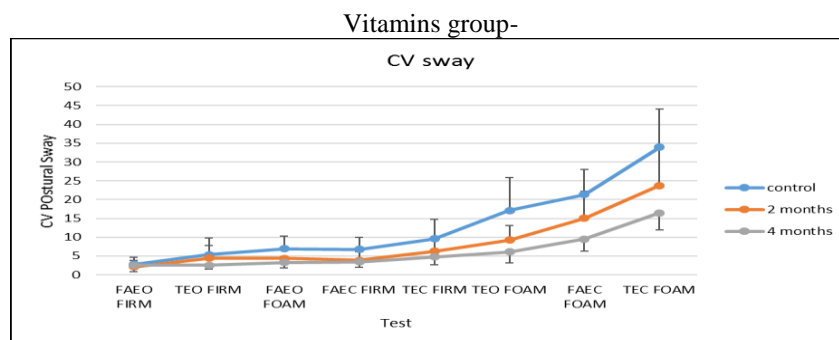


Figure 23- The coefficient of variation of postural sway during 8 balance tasks in all of the subjects under 3 conditions; start, after 2 months and after 4 months for the subjects using vitamins. Each point is the mean of 20 subjects +/- the SD.

There was significantly less sway comparing the 2 month to control data when examining sway in the 6 more difficult balance tasks ($p < 0.01$) (Figure 23). For the easier tasks, there was no significant difference comparing

control to 2 months. But by the 4th month, everything above the easiest task showed significantly less sway ($p < 0.01$ ANOVA) than was seen at the start of the study. The 2-month sway data was significantly greater than the 4-month sway data (ANOVA $p < 0.01$). For the most difficult task, for example, with the subject standing tandem on foam with eyes closed, there was a 17.4 % reduction in the coefficient of variation of sway from the start to the 4-month measurement.

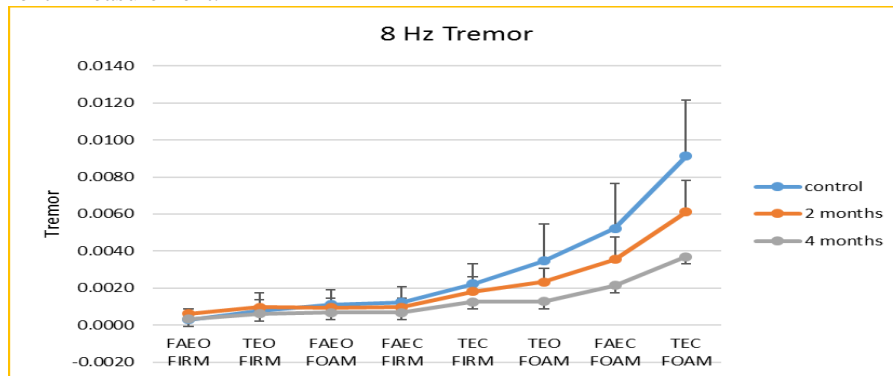


Figure 24- The tremor during the 8 balance tasks in all subjects at 3 times; start, after 2 months and after 4 months in subjects using vitamins. Each point is the mean of 20 subjects +/- the SD.

In the 6-10 Hz bandwidth, tremor increased significantly in the heat group for the 4 most difficult balance tasks ($p < .01$) (Figure 24) but was reduced significantly on the last 2 measurement periods after vitamins were used ($p < 0.01$). By the 4th month after taking vitamins, the 6 most difficult tasks showed significantly less tremor than in the first month (ANOVA $p < 0.01$).

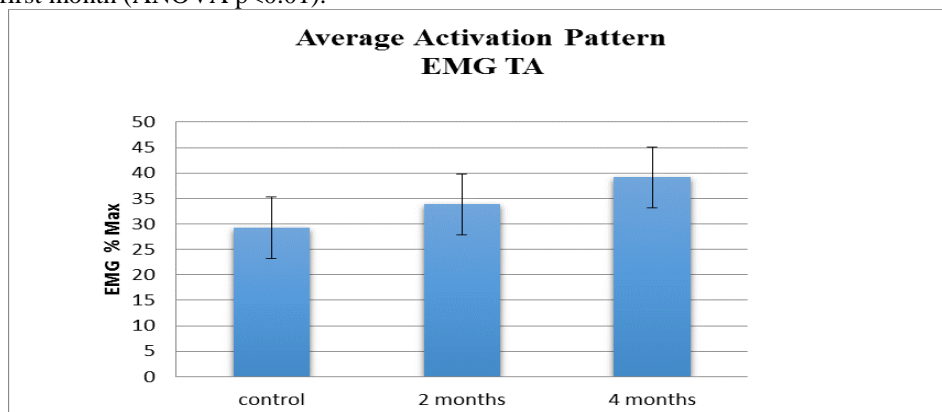


Figure 25- The muscle activity of the tibialis anterior in the vitamin only subjects at the start, after 2 months and after 4 months. Each point is the mean of 20 subjects +/- the SD.

The EMG of the tibialis anterior at the start, after 2 months and 4 months on vitamins is shown in Figure 25. Figure 26 and 27 show the EMG activity in the quadriceps and the vastus lateralis. For all 3 muscle groups, muscle activity was significantly higher at 2 and 4 months after ingesting vitamins (ANOVA $p < 0.01$). The increase from the start of the study was about 25%.

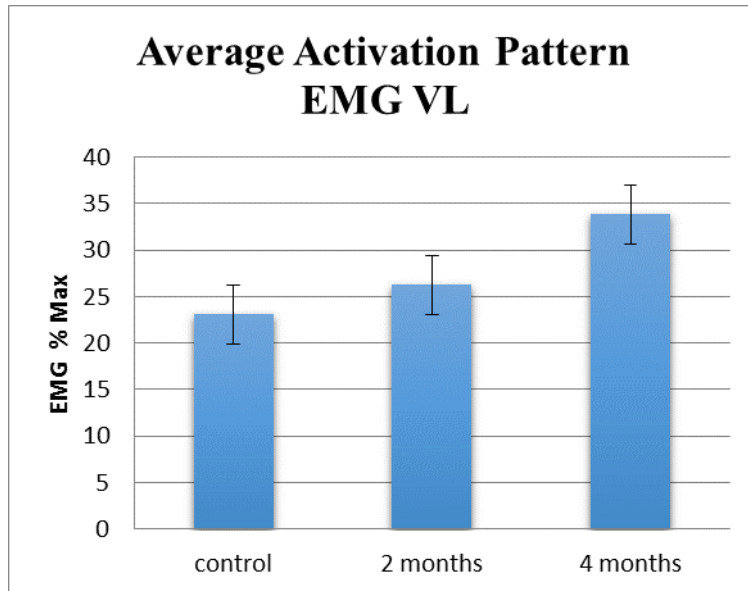


Figure 26 -The muscle activity of the vastus lateralis in the vitamin only subjects at the start, after 2 months and after 4 months. Each point is the mean of 20 subjects +/- the SD.

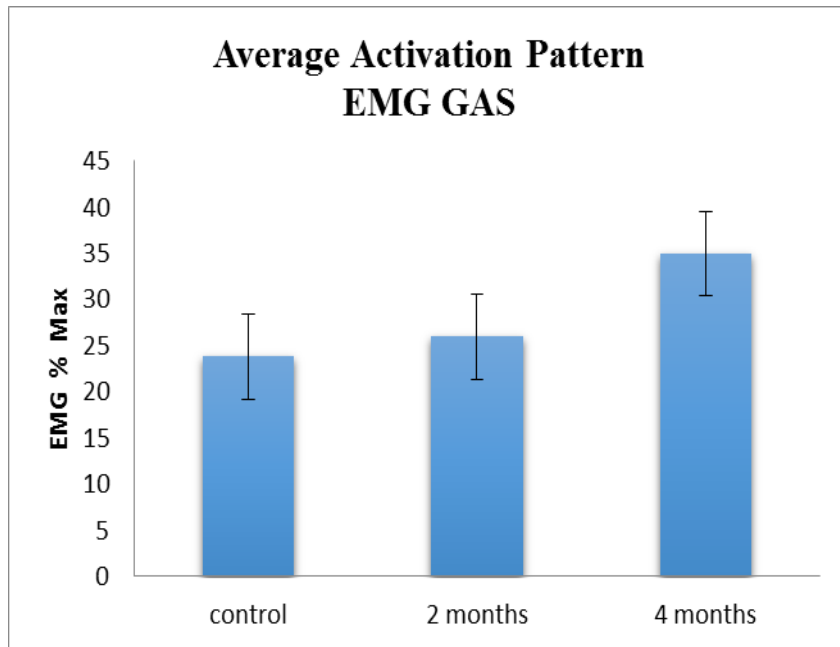


Figure 27 - The muscle activity of the gastrocnemius in the vitamin only subjects at the start, after 2 months and after 4 months. Each point is the mean of 20 subjects +/- the SD.

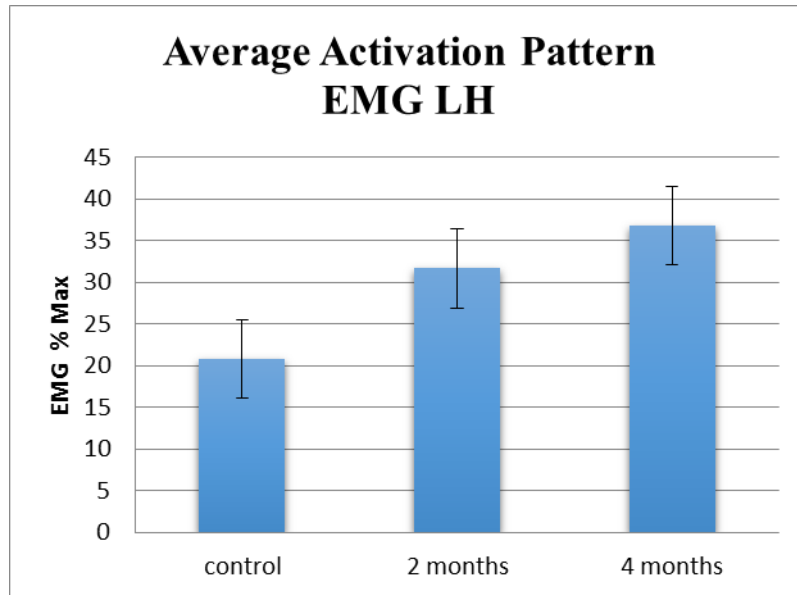


Figure 28- The EMG activity in the left hamstring at the start and after 2 and 4 months in the vitamin only group. Each point is the mean of 20 subjects +/- the SD.

The same was true for the lower leg as shown in Figure 28 where the muscle activity of the left hamstring muscle increased in the first 2 months and after 4 months significantly after taking vitamins. In summary, as shown in these 4 figures, there was a significant increase in muscle activity at the knee after 2 months on vitamins.

	Spatial Parameters			Temporal Parameter		
	Step Length	Stride length	Step Width	Step Time	Stride Time	Cadence
start	53.3	107.2	12.7	0.6	1.3	97.4
SD	4.4	8.4	3.3	0.0	0.1	7.7
2 months	51.7	104.5	12.9	0.6	1.2	100.4
SD	3.4	7.3	3.1	0.0	0.1	7.5
4 months	50.2	101.8	13.1	0.6	1.2	103.4
SD	4.3	7.5	3.7	0.0	0.1	9.2

Table 5- temporal and spatial characteristics of gait in the vitamin group. Each point is the mean of 20 subjects +/- the SD. As shown in Table 5, the gait increased in speed in the last 2 periods after taking vitamins.

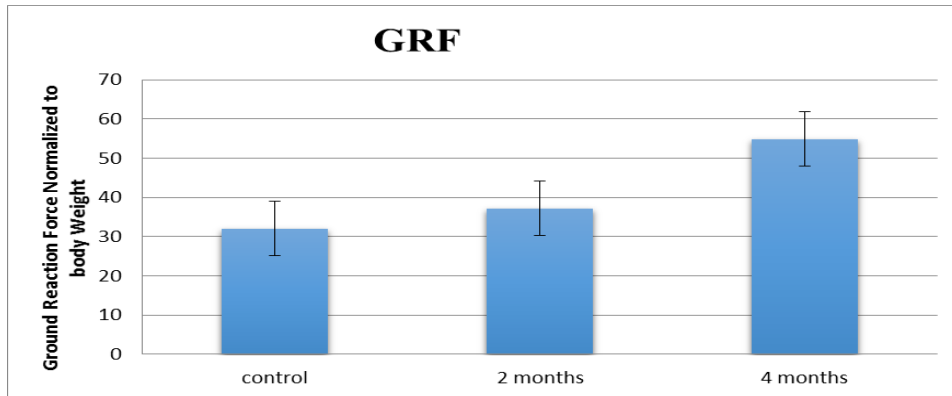


Figure 29- Ground reaction force in the vitamin only group at the start, after 2 months and after 4 months. Each point is the mean of 20 subjects +/- the SD.

As shown in figure 29, the ground reaction forces on the feet increased with muscle activity in the 4 months on vitamins.

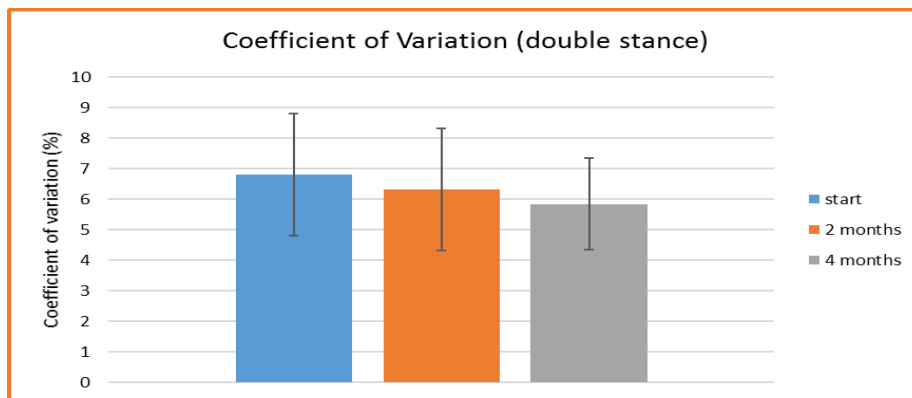


Figure 30- The gait symmetry (coefficient of variation of the center of pressure in double stance) in the subjects in the vitamin subjects at the beginning and after 2 and 4 months. Data is the mean +/- the standard deviation of the group for the single stance phase in the vitamin group.

As shown in Figure 30, there was a reduction in the coefficient of variation of the center of pressure which was not significant comparing start to 2 months, was significant by 4 months. The reduction in the variation in center of pressure was about 20%.

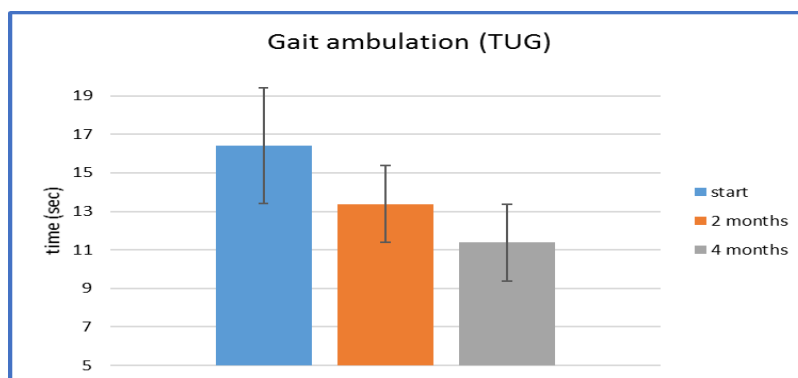


Figure 31- The Time up and go at the beginning, after 2 months and after 4 months. Data is the mean +/- the standard deviation of the group for the double stance phase in the vitamin group.

As illustrated in Figure 31, the time up and go time significantly ($p < 0.01$) decreased in the first 2 months and at 4 months. The decrease from the 2nd to 4th month was also significant showing a continued effect of the vitamins.

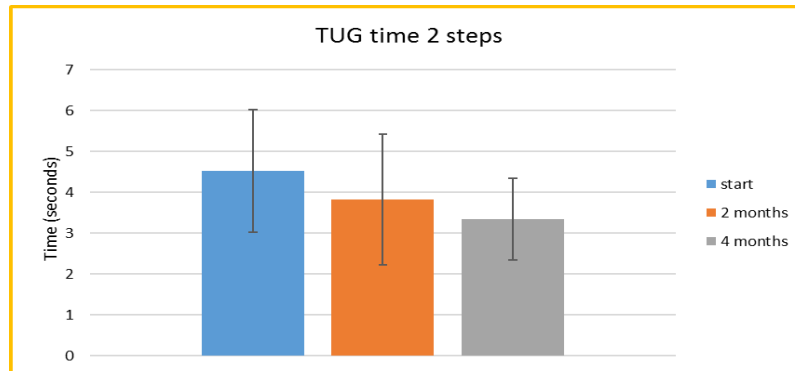


Figure 32- The time for the first 2 steps at the start, after 2 months and after 4 months in the vitamin group. Data is the mean +/- the standard deviation of the group taking vitamins.

Not only was the TUG faster but the initial stand-up time for the first 2 steps was also reduced significantly after 2 months (Figure 32) ($p < 0.05$) and 4 months ($p < 0.01$). This showed faster muscle acceleration and strength after 4 month compared to the control data. Compliance for Vitamins The vitamins taken each day for the 4-month period were monitored and the compliance for taking the vitamins was assessed. For the group, the average compliance was 92.8 +/- 4.3 %. This was a very good compliance.

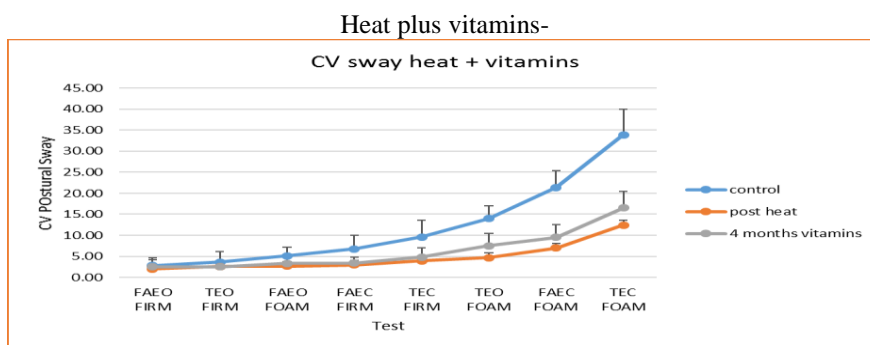


Figure 33- The coefficient of variation of postural sway during 8 balance tasks in all of the subjects under 3 conditions; start, after 2 months and after 4 months in subjects using vitamins and heat. Each point is the mean of 20 subjects +/- the SD.

There was significantly less sway comparing the 4 month to control data when examining sway in the 4 more difficult balance tasks ($p < 0.01$) (Figure 33). It was interesting that there was no significant difference between the vitamins only group and the vitamins and heat group at the 4-month point for any of the 8 tests (ANOVA $p > 0.05$). However, heat for 2 week caused a significant reduction in sway at the most difficult balance tasks (Figure 33 $p < 0.01$)

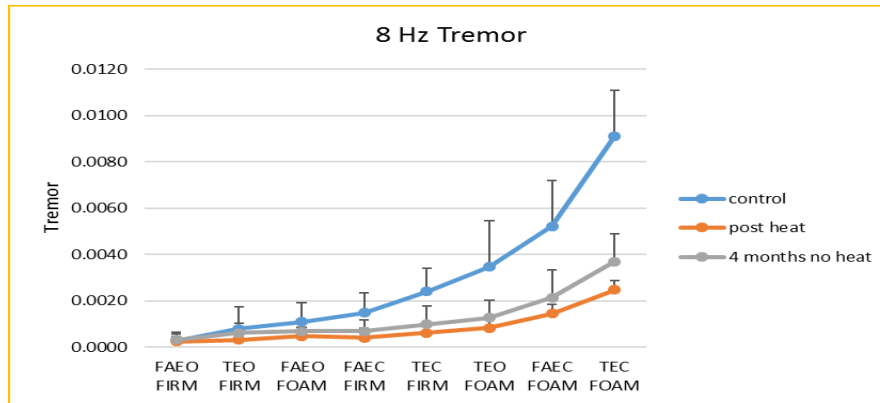


Figure 34- The tremor during the 8 balance tasks in all subjects at 3 times; start, after 2 months and after 4 months in subjects using vitamins. Each point is the mean of 20 subjects +/- the SD.

In the 6-10 Hz bandwidth, tremor increased significantly in the heat group for the 4 most difficult balance tasks ($p < .01$) (Figure 34) but was reduced significantly after 4 months after vitamins were used ($p < 0.01$). While there was no difference for tremor at any of the 8 tasks comparing the vitamin group to the vitamin group at 4 months and before heat (ANOVA $p > 0.05$), heat reduced tremor even more for all balanced tasks.

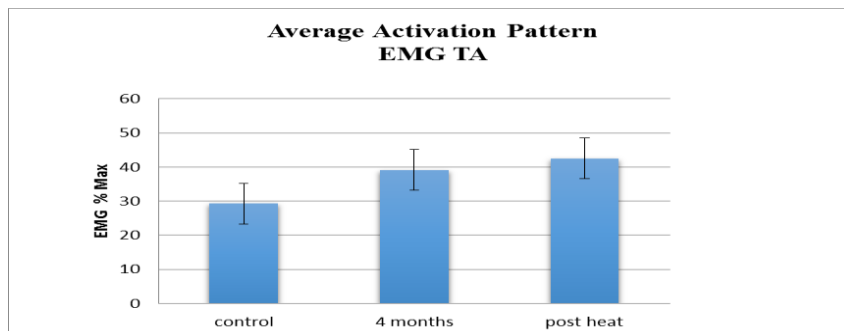


Figure 35- The muscle activity of the tibialis anterior in the vitamin and heat subjects at the start, after 4 months and after heat for 2 weeks. Each point is the mean of 20 subjects +/- the SD.

The EMG of the tibialis anterior at the start, after 4 months on vitamins and after heat is shown in Figure 35. As shown here, there was a significant increase in muscle activity after 4 months on vitamins and after heat compared to the control data. Figure 36 and 37 show the EMG activity in the vastus lateralis and gastrocnemius muscles.

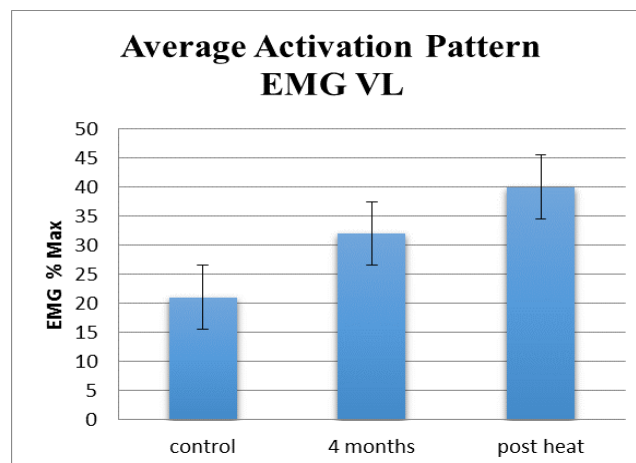


Figure 36 -The muscle activity of the vastus lateralis in the vitamin and heat subjects at the start, after 4 months and after heat. Each point is the mean of 20 subjects +/- the SD.

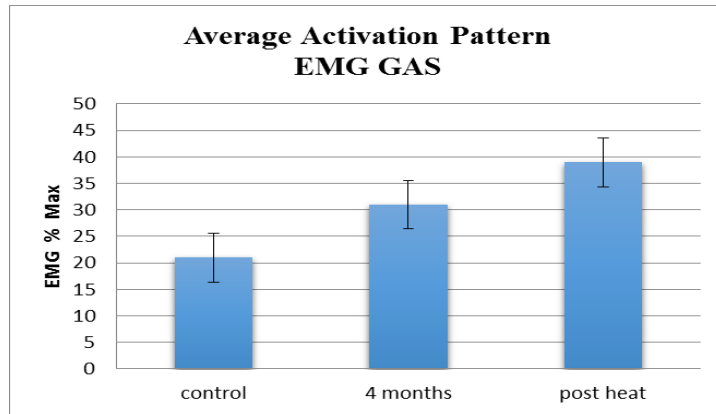


Figure 37 - The muscle activity of the gastrocnemius in the vitamin and heat subjects at the start, after 4 months and post heat. Each point is the mean of 20 subjects +/- the SD.

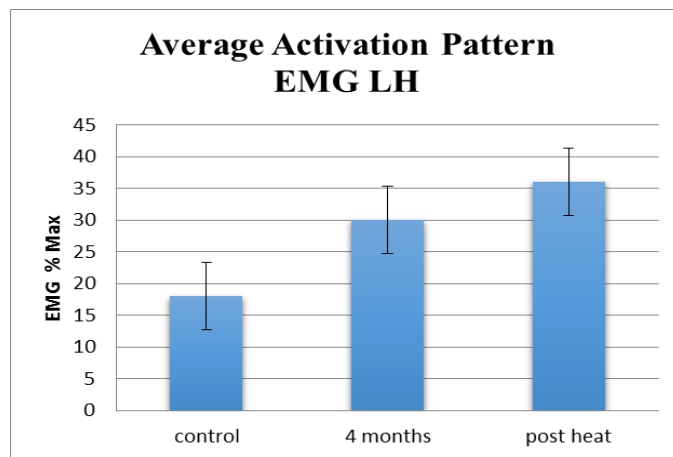


Figure 38- The EMG activity in the lateral hamstring at the start and after 4 months and after heat in the vitamin and heat group. Each point is the mean of 20 subjects +/- the SD.

	Spatial Parameters			Temporal Parameter		
	Step Length	Stride length	Step Width	Step Time	Stride Time	Cadence
start	53.5	106.7	11.8	0.55	1.4	96.3
SD	4.1	8.1	2.3	0.0	0.1	6.7
4 months	49.2	100.3	14.1	0.54	1.2	104.1
SD	3.9	7.7	3.9	0.0	0.1	7.7
Post heat	47.2	98.3	15.1	0.53	1.1	106.1
SD	3.7	7.1	4.1	0.0	0.1	7.9

Table 6- temporal and spatial characteristics of gait in the vitamin and heat group. Each point is the mean of 20 subjects +/- the SD.

As shown in Table 5, the gait increased in speed after vitamins and after heat was applied.

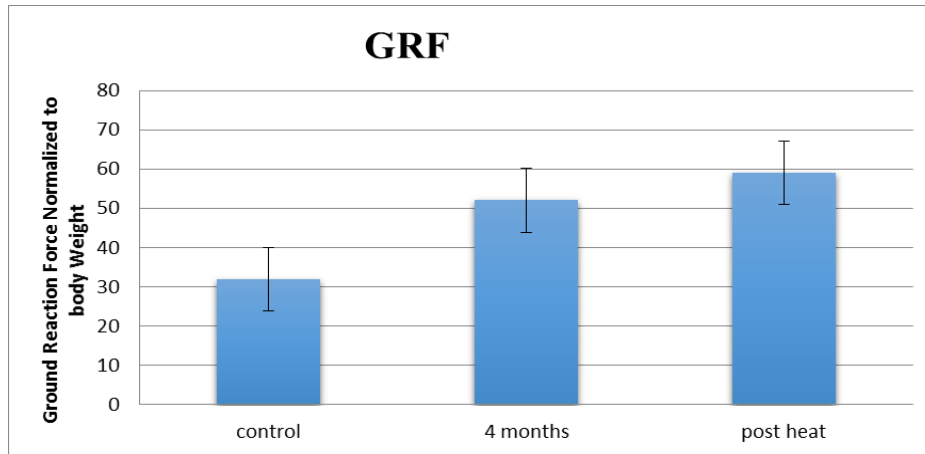


Figure 39- Ground reaction force in the vitamin and heat group at the start, after 4 months and after heat. Each point is the mean of 20 subjects +/- the SD.

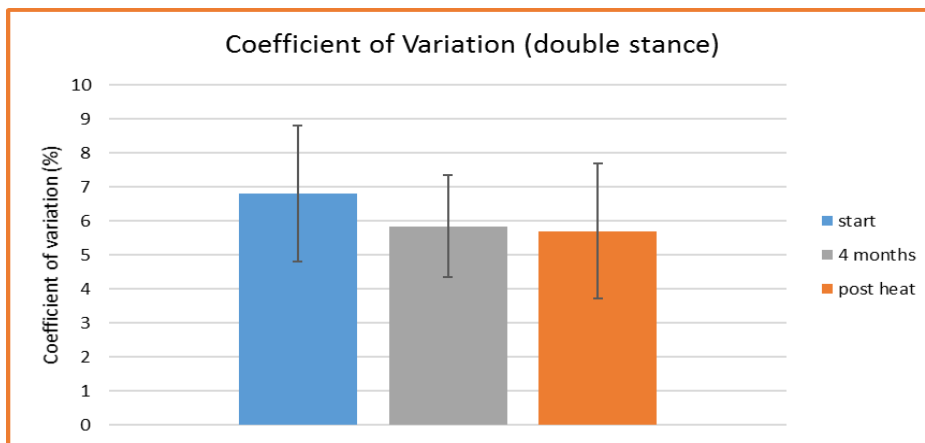


Figure 40- The gait symmetry (coefficient of variation of the center of pressure in double stance) in the subjects in the vitamin subjects at the beginning and after 2 and 4 months. Data is the mean +/- the standard deviation of the group for the single stance phase.

As shown in Figure 40, there was a reduction in the coefficient of variation of the center of pressure which was not significant comparing start to 2 months.

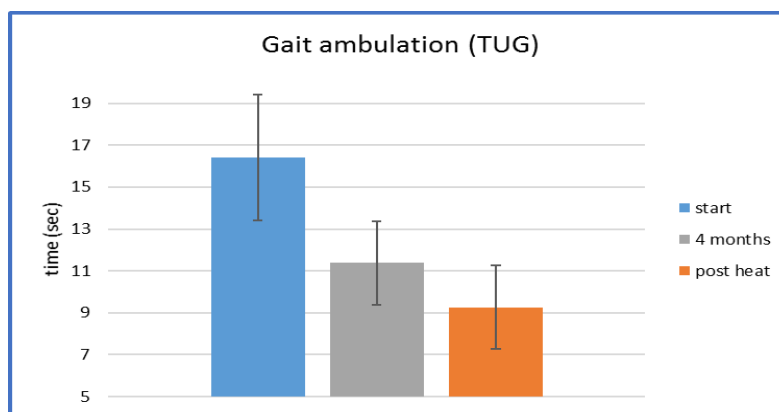


Figure 41- The Time up and go at the beginning, after 2 months and after 4 months. Data is the mean +/- the standard deviation of the group for the double stance phase.

As illustrated in Figure 41, the time up and go time significantly ($p < 0.01$) decreased in the first 2 months.

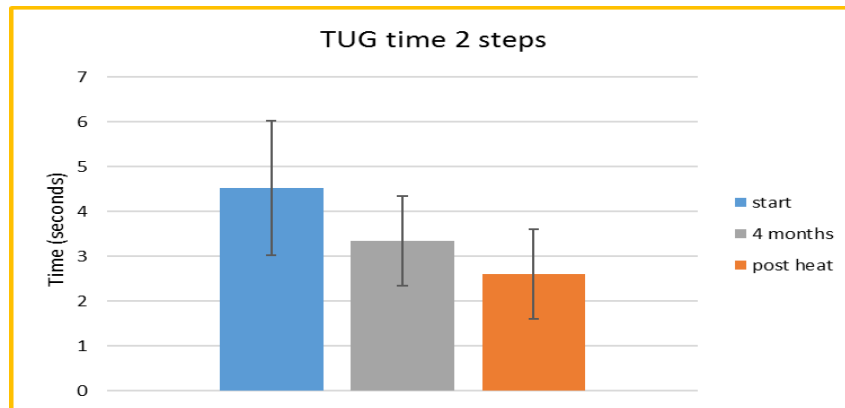


Figure 42- The time for the first 2 steps at the start, after 2 months and after 4 months in the vitamin group. Data is the mean +/- the standard deviation of the group.

Not only was the TUG faster but the initial stand-up time was also reduced significantly after 2 months ($p < 0.05$).

Bone Density- In one of the groups of 20 subjects, vitamins were given for 4 months and bone density was measured before and after the 4-month period of ingesting vitamins and calcium. The results showed that for the group, the mean T score started at -0.564 ± 1.4 and increased to -0.25 ± 1.49 at the end of the 4 months, a significant improvement ($p = 0.03$).

Compliance for vitamins and heat- The average compliance for taking the vitamins was $92.1 \pm 3.9\%$ and for using the heat for the 10 days was $94.7 \pm 9.6\%$. Thus compliance was very good for both in these subjects.

VII. DISCUSSION

There is a natural senescence of the nervous system as people age [72]. This includes changes in nerve conduction speed and changes in the collagen in joints and skin [73]. The overall result is a slowing in gait and increase in tremor associated with the ageing process. Gait changes include slower gait, wider stance and increase in tremor [74-76]. In addition, there is an overall increase in inflammation in the body including muscle and tendons associated with ageing [77]. There is evidence that the chronic inflammation associated with ageing is causative of the increase in heart disease and sarcopenia seen with ageing [78, 79]. Individuals who have a good diet, high in antioxidants, have less mobility issues and live longer than poor eating counterparts. Therefore, many studies have examined various dietary supplements to see if taking these has been associated with increased health and better mobility [80-82]. A number of studies have examined the effect of vitamin D on mobility. While some studies show little effect on falls, a recent review of 8 studies with a meta-analysis showed that falls were reduced when vitamin D was ingested at 800 IU per day [39-44]. Sarcopenia is a well known symptom (proximal) of vitamin D deficiency [45, 46]. There are vitamin D receptors in skeletal muscle that cause muscle to build strength [47-49]. In the present investigation, we are in agreement with these studies showing increase in stability and speed of gait and better balance in people taking vitamin D. But antioxidants also may have a role. For example, a diet high in Co Q10 has been shown to reverse the endothelial damage associated with eating high fat meals in Asians [32, 33, 55]. It also has been shown to reduce oxidative stress in the eye [83, 84] and can reduce fatigue [85]. Q10 is necessary for carbohydrate metabolism as well as lipid metabolism, adding energy to the cell [86]. It is depleted in older individuals and people taking statins [87]. When q10 in the plasma is low, muscle wasting and cramping can be seen [88, 89]. Here, large doses of q10 were used that normally increase cardiac health and certainly contributed to the results seen here. The B vitamins also modulate carbohydrate metabolism [90]. When low in seniors, they are associated with depression [90-92]. This is true of several other b vitamins. Here, multivitamins supplemented B vitamin status and may also contribute to increased mobility. Everything added together, it is not surprising that there was a significant increase in mobility and balance in these seniors. It was interesting that the increase was significant even after 2 months. But this group was vitamin naive and therefore were probably very low on vitamin D and

calcium and the B vitamins. Subjects reported increased energy and a feeling of well-being after 4 months. It was also of interest that their bone density increased after 4 months. Vitamins alone increased mobility and balance. Heat alone increased mobility and balance. The 2 together were synergistic and increased balance and mobility even more. The primary effect of the heat wraps would be to increase metabolism in the tissue and increase fluidity in the tendons and ligaments. For heat, this would explain the increase in mobility and balance. For the vitamins, the decrease in cellular inflammation would also seem to increase mobility. Whatever the mechanism, the vitamin dosage used here was just as effective as heat alone. But the 2 used together would be better.

BIBLIOGRAPHY

- [1] Tinetti, M.E. and M. Speechley, Prevention of falls among the elderly. *N Engl J Med*, 1989. **320**(16): p. 1055-9.
- [2] Hausdorff, J.M., D.A. Rios, and H.K. Edelberg, Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Arch Phys Med Rehabil*, 2001. **82**(8): p. 1050-6.
- [3] Jorgensen, T.S., et al., Nationwide time trends and risk factors for in-hospital falls-related major injuries. *Int J Clin Pract*, 2015.
- [4] Scott, V.J. and E.M. Gallagher, Mortality and morbidity related to injuries from falls in British Columbia. *Can J Public Health*, 1999. **90**(5): p. 343-7.
- [5] Tinetti, M.E., et al., Fear of falling and fall-related efficacy in relationship to functioning among community-living elders. *J Gerontol*, 1994. **49**(3): p. M140-7.
- [6] Arfken, C.L., et al., The prevalence and correlates of fear of falling in elderly persons living in the community. *Am J Public Health*, 1994. **84**(4): p. 565-70.
- [7] Fernie, G.R., et al., The relationship of postural sway in standing to the incidence of falls in geriatric subjects. *Age Ageing*, 1982. **11**(1): p. 11-6.
- [8] Baker, S.P. and A.H. Harvey, Fall injuries in the elderly. *Clin Geriatr Med*, 1985. **1**(3): p. 501-12.
- [9] Petrofsky, J.S. and A.R. Lind, Aging, isometric strength and endurance, and cardiovascular responses to static effort. *J Appl Physiol*, 1975. **38**(1): p. 91-5.
- [10] Schalow, G., Time axis calibration in human CNS organization for judging dysfunction. *Electromyogr Clin Neurophysiol*, 2001. **41**(8): p. 485-505.
- [11] Dowiasch, S., et al., Effects of aging on eye movements in the real world. *Front Hum Neurosci*, 2015. **9**: p. 46.
- [12] Mueller, M.J., et al., Differences in the gait characteristics of patients with diabetes and peripheral neuropathy compared with age-matched controls. *Phys Ther*, 1994. **74**(4): p. 299-308; discussion 309-13.
- [13] Moreira, B.S., R.F. Sampaio, and R.N. Kirkwood, Spatiotemporal gait parameters and recurrent falls in community-dwelling elderly women: a prospective study. *Braz J Phys Ther*, 2015. **19**(1): p. 61-9.
- [14] Dohrn, I.M., et al., Gait Speed, Quality of Life, and Sedentary Time are Associated With Steps Per Day in Community-Dwelling Older Adults With Osteoporosis. *J Aging Phys Act*, 2015.
- [15] Bridenbaugh, S.A. and R.W. Kressig, Motor cognitive dual tasking : Early detection of gait impairment, fall risk and cognitive decline. *Z Gerontol Geriatr*, 2015. **48**(1): p. 15-21.
- [16] Gillespie, L.D., et al., Interventions for preventing falls in elderly people. *Cochrane Database Syst Rev*, 2003(4): p. CD000340.
- [17] Laymon, M., et al., Effect of heat, cold, and pressure on the transverse carpal ligament and median nerve: a pilot study. *Med Sci Monit*, 2015. **21**: p. 446-51.
- [18] Lee, H., et al., Anterior cruciate ligament elasticity and force for flexion during the menstrual cycle. *Med Sci Monit*, 2013. **19**: p. 1080-8.
- [19] Lee, H., et al., Differences in anterior cruciate ligament elasticity and force for knee flexion in women: oral contraceptive users versus non-oral contraceptive users. *Eur J Appl Physiol*, 2014. **114**(2): p. 285-94.
- [20] Lee, H., et al., A greater reduction of anterior cruciate ligament elasticity in women compared to men as
- [21] Khowailed, I.A., et al., 17beta-Estradiol Induced Effects on Anterior Cruciate Ligament Laxness and Neuromuscular Activation Patterns in Female Runners. *J Womens Health (Larchmt)*, 2015.
- [22] Khowailed, I.A., et al., Six Weeks Habituation of Simulated Barefoot Running Induces Neuromuscular Adaptations and Changes in Foot Strike Patterns in Female Runners. *Med Sci Monit*, 2015. **21**: p. 2021-30.
- [23] Petrofsky, J., et al., Moist heat or dry heat for delayed onset muscle soreness. *J Clin Med Res*, 2013. **5**(6): p. 416-25.
- [24] Petrofsky, J.S., M. Laymon, and H. Lee, Effect of heat and cold on tendon flexibility and force to flex the human knee. *Med Sci Monit*, 2013. **19**: p. 661-7.

- [25] Petrofsky, J., et al., The interrelationship between locally applied heat, ageing and skin blood flow on heat transfer into and from the skin. *J Med Eng Technol*, 2011. **35**(5): p. 262-74.
- [26] Petrofsky, J., et al., Does skin moisture influence the blood flow response to local heat? A re-evaluation of the Pennes model. *J Med Eng Technol*, 2009. **33**(7): p. 532-7.
- [27] Petrofsky, J.S., et al., The influence of ageing on the ability of the skin to dissipate heat. *Med Sci Monit*, 2009. **15**(6): p. CR261-8.
- [28] Petrofsky, J.S., et al., The influence of local versus global heat on the healing of chronic wounds in patients with diabetes. *Diabetes Technol Ther*, 2007. **9**(6): p. 535-44.
- [29] Malanga, G.A., N. Yan, and J. Stark, Mechanisms and efficacy of heat and cold therapies for musculoskeletal injury. *Postgrad Med*, 2015. **127**(1): p. 57-65.
- [30] Petrofsky, J.S., et al., Effect of ThermaCare HeatWraps and Icy Hot Cream/Patches on Skin and Quadriceps Muscle Temperature and Blood Flow. *J Chiropr Med*, 2016. **15**(1): p. 9-18.
- [31] Petrofsky, J.S., et al., Use of low level of continuous heat as an adjunct to physical therapy improves knee pain recovery and the compliance for home exercise in patients with chronic knee pain: a randomized controlled trial. *J Strength Cond Res*, 2016.
- [32] Yim, J., et al., Protective effect of anti-oxidants on endothelial function in young Korean-Asians compared to Caucasians. *Med Sci Monit*, 2012. **18**(8): p. CR467-479.
- [33] Yim, J., et al., Differences in endothelial function between Korean-Asians and Caucasians. *Med Sci Monit*, 2012. **18**(6): p. CR337-43.
- [34] Kim, H.J., et al., Association between serum vitamin D status and health-related quality of life (HRQOL) in an older Korean population with radiographic knee osteoarthritis: data from the Korean national health and nutrition examination survey (2010-2011). *Health Qual Life Outcomes*, 2015. **13**: p. 48.
- [35] Park, Y.E., et al., Vitamin D status of patients with early inflammatory arthritis. *Clin Rheumatol*, 2015. **34**(2): p. 239-46.
- [36] Patil, R., et al., Cost-effectiveness of vitamin D supplementation and exercise in preventing injurious falls among older home-dwelling women: findings from an RCT. *Osteoporos Int*, 2015.
- [37] Uusi-Rasi, K., et al., Exercise and vitamin D in fall prevention among older women: a randomized clinical trial. *JAMA Intern Med*, 2015. **175**(5): p. 703-11.
- [38] Anagnostis, P., et al., Sarcopenia in post-menopausal women: Is there any role for vitamin D? *Maturitas*, 2015.
- [39] Bischoff-Ferrari, H., H.B. Stahelin, and P. Walter, Vitamin D effects on bone and muscle. *Int J Vitam Nutr Res*, 2011. **81**(4): p. 264-72.
- [40] Bischoff-Ferrari, H.A., B. Dawson-Hughes, and S.J. Whiting, Vitamin D supplementation and fracture risk. *Arch Intern Med*, 2011. **171**(3): p. 265; author reply 265-6.
- [41] Bischoff-Ferrari, H.A., et al., Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. *BMJ*, 2009. **339**: p. b3692.
- [42] Bischoff-Ferrari, H.A., et al., Is fall prevention by vitamin D mediated by a change in postural or dynamic balance? *Osteoporos Int*, 2006. **17**(5): p. 656-63.
- [43] Bruyere, O., et al., Effects of vitamin D in the elderly population: current status and perspectives. *Arch Public Health*, 2014. **72**(1): p. 32.
- [44] Beaudart, C., et al., The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab*, 2014. **99**(11): p. 4336-45.
- [45] Al-Shoha, A., et al., Osteomalacia with bone marrow fibrosis due to severe vitamin D deficiency after a gastrointestinal bypass operation for severe obesity. *Endocr Pract*, 2009. **15**(6): p. 528-33.
- [46] Schott, G.D. and M.R. Wills, Muscle weakness in osteomalacia. *Lancet*, 1976. **1**(7960): p. 626-9.
- [47] Bischoff-Ferrari, H.A., et al., Vitamin D receptor expression in human muscle tissue decreases with age. *J Bone Miner Res*, 2004. **19**(2): p. 265-9.
- [48] Ceglia, L., et al., Multi-step immunofluorescent analysis of vitamin D receptor loci and myosin heavy chain isoforms in human skeletal muscle. *J Mol Histol*, 2010. **41**(2-3): p. 137-42.
- [49] Girgis, C.M., et al., The roles of vitamin D in skeletal muscle: form, function, and metabolism. *Endocr Rev*, 2013. **34**(1): p. 33-83.
- [50] Flores, M., A role of vitamin D in low-intensity chronic inflammation and insulin resistance in type 2 diabetes mellitus? *Nutr Res Rev*, 2005. **18**(2): p. 175-82.
- [51] Slusher, A.L., M.J. McAllister, and C.J. Huang, A therapeutic role for vitamin D on obesity-associated inflammation and weight-loss intervention. *Inflamm Res*, 2015. **64**(8): p. 565-75.
- [52] Mutt, S.J., et al., Vitamin D and adipose tissue-more than storage. *Front Physiol*, 2014. **5**: p. 228.
- [53] Mutti, D.O., Vitamin D may reduce the prevalence of myopia in Korean adolescents. *Invest Ophthalmol Vis Sci*, 2014. **55**(4): p. 2048.

- [54] Vix, M., et al., Impact of Roux-en-Y gastric bypass versus sleeve gastrectomy on vitamin D metabolism: short-term results from a prospective randomized clinical trial. *Surg Endosc*, 2014. **28**(3): p. 821-6.
- [55] Petrofsky, J., et al., The effect of acute administration of vitamin D on micro vascular endothelial function in Caucasians and South Asian Indians. *Med Sci Monit*, 2013. **19**: p. 641-7.
- [56] Castro-Marrero, J., et al., Does oral coenzyme Q10 plus NADH supplementation improve fatigue and biochemical parameters in chronic fatigue syndrome? *Antioxid Redox Signal*, 2015. **22**(8): p. 679-85.
- [57] Bui, C., et al., Acute effect of a single high-fat meal on forearm blood flow, blood pressure and heart rate in healthy male Asians and Caucasians: a pilot study. *Southeast Asian J Trop Med Public Health*, 2010. **41**(2): p. 490-500.
- [58] Petrofsky, J.S., et al., Reduced endothelial function in the skin in Southeast Asians compared to Caucasians. *Med Sci Monit*, 2012. **18**(1): p. CR1-8.
- [59] Venkata Subbaiah, K.C., et al., Newcastle disease virus (NDV) induces protein oxidation and nitration in brain and liver of chicken: Ameliorative effect of vitamin E. *Int J Biochem Cell Biol*, 2015. **64**: p. 97-106.
- [60] Muniz, F.W., et al., The impact of antioxidant agents complimentary to periodontal therapy on oxidative stress and periodontal outcomes: A systematic review. *Arch Oral Biol*, 2015. **60**(9): p. 1203-1214.
- [61] Fusco, D., et al., Effects of antioxidant supplementation on the aging process. *Clin Interv Aging*, 2007. **2**(3): p. 377-87.
- [62] Rubenstein, L.Z., et al., Validating an evidence-based, self-rated fall risk questionnaire (FRQ) for older adults. *J Safety Res*, 2011. **42**(6): p. 493-9.
- [63] Clark, S. and M.A. Riley, Multisensory information for postural control: sway-referencing gain shapes center of pressure variability and temporal dynamics. *Exp Brain Res*, 2007. **176**(2): p. 299-310.
- [64] Kouzaki, M. and M. Shinohara, Steadiness in plantar flexor muscles and its relation to postural sway in young and elderly adults. *Muscle Nerve*, 2010. **42**(1): p. 78-87.
- [65] Petrofsky, J.S., E. Lohman, and T. Lohman, A device to evaluate motor and autonomic impairment. *Med Eng Phys*, 2009. **31**(6): p. 705-12.
- [66] Tse, Y.Y., et al., Postural sway and rhythmic electroencephalography analysis of cortical activation during eight balance training tasks. *Med Sci Monit*, 2013. **19**: p. 175-86.
- [67] Coulthard, J.T., et al., Evaluation of an inertial sensor system for analysis of timed-up-and-go under dual-task demands. *Gait Posture*, 2015.
- [68] Kojima, G., et al., Does the timed up and go test predict future falls among British community-dwelling older people? Prospective cohort study nested within a randomised controlled trial. *BMC Geriatr*, 2015. **15**(1): p. 38.
- [69] Davis, J.C., et al., Examining the effect of the relationship between falls and mild cognitive impairment on mobility and executive functions in community-dwelling older adults. *J Am Geriatr Soc*, 2015. **63**(3): p. 590-3.
- [70] Davis, J.C., et al., Mobility is a key predictor of changes in wellbeing among older fallers: Evidence from the Vancouver Falls Prevention Cohort. *Arch Phys Med Rehabil*, 2015.
- [71] Fasano, A., et al., The neurobiology of falls. *Neurol Sci*, 2012. **33**(6): p. 1215-23.
- [72] Petrofsky, J. and S. Lee, The effects of type 2 diabetes and aging on vascular endothelial and autonomic function. *Med Sci Monit*, 2005. **11**(6): p. CR247-254.
- [73] Berridge, M.J., Vitamin D, reactive oxygen species and calcium signalling in ageing and disease. *Philos Trans R Soc Lond B Biol Sci*, 2016. **371**(1700).
- [74] Petrofsky, J.S., et al., Correlation between gait and balance in people with and without Type 2 diabetes in normal and subdued light. *Med Sci Monit*, 2006. **12**(7): p. CR273-81.
- [75] Petrofsky, J., et al., Autonomic, endothelial function and the analysis of gait in patients with type 1 and type 2 diabetes. *Acta Diabetol*, 2005. **42**(1): p. 7-15.
- [76] Petrofsky, J.S., et al., Joint acceleration during gait in relation to age. *Eur J Appl Physiol*, 2004. **92**(3): p. 254-62.
- [77] Bandaranayake, T. and A.C. Shaw, Host Resistance and Immune Aging. *Clin Geriatr Med*, 2016. **32**(3): p. 415-32.
- [78] Batsis, J.A., et al., Sarcopenia, sarcopenic obesity and inflammation: Results from the 1999-2004 National Health and Nutrition Examination Survey. *Clin Nutr*, 2016.
- [79] Germain, C.M., et al., Muscle Strength, Physical Activity, and Functional Limitations in Older Adults with Central Obesity. *J Aging Res*, 2016. **2016**: p. 8387324.
- [80] Strike, S.C., et al., A High Omega-3 Fatty Acid Multinutrient Supplement Benefits Cognition and Mobility in Older Women: A Randomized, Double-blind, Placebo-controlled Pilot Study. *J Gerontol A Biol Sci Med Sci*, 2016. **71**(2): p. 236-42.

- [81] Fragala, M.S., A.M. Kenny, and G.A. Kuchel, Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. *Sports Med*, 2015. **45**(5): p. 641-58.
- [82] Aqai, P., et al., Receptor-based high-throughput screening and identification of estrogens in dietary supplements using bioaffinity liquid-chromatography ion mobility mass spectrometry. *Anal Bioanal Chem*, 2013. **405**(29): p. 9427-36.
- [83] Lee, D., et al., Coenzyme Q10 inhibits glutamate excitotoxicity and oxidative stress-mediated mitochondrial alteration in a mouse model of glaucoma. *Invest Ophthalmol Vis Sci*, 2014. **55**(2): p. 993-1005.
- [84] Lee, D., et al., Coenzyme Q10 ameliorates oxidative stress and prevents mitochondrial alteration in ischemic retinal injury. *Apoptosis*, 2014. **19**(4): p. 603-14.
- [85] Peel, M.M., et al., A randomized controlled trial of coenzyme Q10 for fatigue in the late-onset sequelae of poliomyelitis. *Complement Ther Med*, 2015. **23**(6): p. 789-93.
- [86] Kennedy, D.O., et al., Multivitamins and minerals modulate whole-body energy metabolism and cerebral blood-flow during cognitive task performance: a double-blind, randomised, placebo-controlled trial. *Nutr Metab (Lond)*, 2016. **13**: p. 11.
- [87] Choi, H.K., E.K. Won, and S.Y. Choung, Effect of Coenzyme Q10 Supplementation in Statin-Treated Obese Rats. *Biomol Ther (Seoul)*, 2016. **24**(2): p. 171-7.
- [88] Banach, M., et al., Statin therapy and plasma coenzyme Q10 concentrations--A systematic review and meta-analysis of placebo-controlled trials. *Pharmacol Res*, 2015. **99**: p. 329-36.
- [89] Banach, M., et al., Effects of coenzyme Q10 on statin-induced myopathy: a meta-analysis of randomized controlled trials. *Mayo Clin Proc*, 2015. **90**(1): p. 24-34.
- [90] O'Leary, F. and S. Samman, Vitamin B12 in health and disease. *Nutrients*, 2010. **2**(3): p. 299-316.
- [91] Edney, L.C., N.R. Burns, and V. Danthiir, Subjective well-being in older adults: folate and vitamin B12 independently predict positive affect. *Br J Nutr*, 2015. **114**(8): p. 1321-8.
- [92] O'Leary, F., M. Allman-Farinelli, and S. Samman, Vitamin B(1)(2) status, cognitive decline and dementia: a systematic review of prospective cohort studies. *Br J Nutr*, 2012. **108**(11): p. 1948-61.