The Effect of Kinetic Dance Training in Brachial Artery Flow-Mediated Dilatation After Chronic Stroke.

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THESIS

Submitted as partial fulfillment of the requirements
for the degree of Masters of Sciences in Rehabilitation Sciences
in the Graduate College of
the University of Illinois at Chicago, 2016

Chicago, Illinois

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This thesis is dedicated to my parents (Mrs. Wasmiah Alshammari and Mr. Younies Alshammari), without whom it would never have been accomplished.

Acknowledgement

First of all, I would thank God, the Almighty, for giving me strength and courage to complete this work and having made everything possible.

Second, I would like to thank all my thesis committee members (Dr. Shane Phillips(Advisor), Dr. Tanvi Bhatt, and Dr. Yi-Ting Tzen) for their support and assistance to complete this thesis. Without their guidance, this thesis never could have been completed.

A number of individuals involved in data collection and training were extremely helpful I would like to thank them all as well, especially, Savitha Subramaniam, for her unwavering support.

Finally, I would thank my country for offering me this opportunity to complete my graduate studies, my friend Alzahrani who shared every moment of this process, and my family who supported me for the last two years.

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LIST OF ABBREVIATIONS

CVD	Cardiovascular Disease
CV	Cardiovascular
CVA	Cardiovascular accident
ED	Endothelial dysfunction
FMD	Flow Mediated Dilation
NO	Nitric Oxide
eNOS	Endothelial Nitric Oxide Synthase
ERF	Endothelial Relaxing Factor
IRB	Institutional review board
UIC	The University of Illinois at Chicago
mmHg	Millimeter of mercury
ANOVA	Analysis of variance
HR	Heart Rate
BP	Blood Pressure
Bpm	Beat per minute
MOCA	Montreal Cognition Assessment

I. **Summary**

The study of the effect of kinetic dance training on the flow-mediated dilatation (FMD) in patients with chronic stroke is a cross-sectional quasi-experimental study. The aim of the study is to investigate the effects of aerobic exercise training (using kinetic dance application of Xbox video game) on the vascular health. Specifically, we will test the effects of the intervention on brachial artery endothelium-dependent flow mediated dilation in a cohort of patients with chronic stroke.

Endothelial dysfunction is one of the leading causes of chronic cardiovascular disease leading to major cerebrovascular accidents(CVA) such as stroke (Fan, Unoki, Iwasa, & Watanabe, 2000). Also, reduced endothelial function brachial FMD is predictive of future cardiovascular(CV) events including stroke (Gokce et al. 2003) & (Modena, Bonetti, Coppi, Bursi, & Rossi, 2002). Therefore, a significant effort has been made to test interventions that may lead to improving the cardiovascular health to prevent or minimize potential cardiovascular disease in stroke populations. Measuring vascular health could be attained by various outcome measurements, one of the methods is evaluating the brachial artery FMD through a noninvasive ultrasound technique (Celermajer et al., 1992). This technology has been widely used to test endothelial function and has been proven as a valid and reliable measurement to predict future cardiovascular events (Gokce et al., 2003) & (Shechter, Shechter, Koren-Morag, Feinberg, & Hiersch, 2014). Physical activity and exercise training are primary targets to improve the general health, prevent disease, and improve the vascular function in patients with chronic stroke (S. Billinger, 2010).

Video gaming and virtual reality training have emerged in the rehabilitation strategy as an alternative therapy that combines strength and balance focused physical activity. Studies show

Summary (continued)

that virtual reality training has a significant impact to improves balance (Saposnik et al., 2010), motor control (Laver, George, Thomas, Deutsch, & Crotty, 2011), gait and strength (da Silva Ribeiro et al., 2015). Since video gaming has been introduced in stroke rehabilitation, there has been no research to test its effectiveness on the vascular health. In our study, we examined the effectiveness of aerobic kinetic dance after chronic stroke for six weeks on vascular function; FMD, flow velocity, heart rate, and blood pressure. Although we include vascular flow at rest and during hyperemia, blood pressure, and HR, our primary outcome measure is the brachial artery FMD.

We recruited a total of 11(N=11) patients with chronic stroke who underwent six weeks of dance training compared to a healthy age-matched control group. The training protocol was a kinetic dance for six weeks. In the first two weeks the training was 5 sessions/week, 38.6 min/session., in week 2-3 the training was 5 sessions/week, 45.5 mins/session, and in week 5-6 the training was 2 Sessions/week, 52.42 minutes/ session. Our results showed that kinetic dance training improves brachial artery FMD after two weeks 14.9% and six weeks of training 32.88% in patients with chronic stroke. The brachial artery FMD in patients with chronic stroke was impaired and significantly lower before the training (5.81%±1.62) in comparison to healthy age-matched control (7.62%± 1.65) (P=0.01). However, this impairment was revised after six weeks of training to improve the brachial artery FMD (7.92±2.06) to be not significantly different from age-matched control (7.62±1.65) who did not receive training (P=0.81). Our finding suggests the effectiveness of the virtual kinetic dance training to improve the hemodynamics and brachial artery FMD in patients with chronic stroke after six weeks of training.

II. Introduction

1. Background

1.1 Stroke Background & Statistics

Cerebrovascular accident (CVA) is a vascular injury in one or multiple of the brain's artery leads to a neurological disorder and reduction in the function. There are different types of stroke depends on the cause of the injury. The ischemic CVA is caused by interruption of blood supply to brain tissue by blocking the blood flow inside the artery by a clot. The hemorrhagic stroke occurs by bursting the artery of a blood vessel causing hemorrhage. The blockage or injured artery leads to interpreting the blood flow and nutrition to the brain tissue which leads to neurological disorder. According to the last updated definition of stroke by American Heart Association "stroke is an episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting more or 24 hours or until death" (Sacco et al., 2013). The severity of neurological loss depends on the affected brain tissue and the type of cells.

The risk factors for stroke are classified modifiable or non-modifiable, which could be targeted to prevent or reduce stroke. Well-documented and modifiable risk factors include high blood pressure, tobacco smoking, diabetes, atrial fibrillation, dyslipidemia, carotid artery stenosis, poor diet, physical inactivity, obesity and body fat distribution. The non-modifiable risk factors which also play a role in developing a stroke include gender, age, ethnicity, and genetics (Ingall, 2004). According to the American Heart Association(AHA), stroke kills around 130,000 Americans every year, and it is ranked the fifth leading cause of death in the United States (Ovbiagele et al., 2013). In 2015, the AHA showed that the stroke prevalence between 2009-2012 was 2.6 % estimating of 6.6 million Americans above 20 years of age have had a stroke (Mozaffarian et al., 2015). That data estimated around 795,000 persons experienced new or recurrent stroke, and anticipating from that data indicate that by 2030, an additional 3.4 million Americans 18 years old or above might have a stroke, a 20.5% increase in prevalence from 2012 (Mozaffarian et al., 2015)

2. Related Literature

2.1 Functional and Cardiovascular Reduction in stroke survivors.

Stroke associates with multi-systematic problem including neurological disorder, musculoskeletal disorder, cardiopulmonary disorder, and other systems leading to mild to severe disability. (Duncan, 1994). Stroke survivors suffer from reduction functional independence level, and reduction of daily activities. Therefore, stroke survivors are likely to adopt a sedentary lifestyle that adversely increases the risk of falling and might contribute to developing recurrent stroke and other cardiovascular conditions (Rutten-Jacobs et al., 2013). Physical activity performance varies among stroke survivors and literature have shown that patients with a stroke in community-dwelling settings suffer low physical activity levels and participation (Gebruers, Vanroy, Truijen, Engelborghs, & De Deyn, 2010).

Aerobic capacity deconditioning is a common symptom for patients with stroke. Several studies showed that patients with stroke have lower exercise aerobic capacity (S. A. Billinger, Arena et al., 2014) and an increase in energy expenditure (Potempa et al., 1995). This lower aerobic capacity leads to a reduction of physical activity which leads to functional deterioration. Aerobic exercise training could improve the aerobic capacity for stroke survivors and reduce the energy expenditure. Treadmill training interventions show promise in the literature to improve the aerobic and cardiovascular capacity in patients with chronic stroke. (Macko et al., 1997). As a result, aerobic training plays a vital role to control and minimize the risk factors and preventing recurrent stroke.

2.2 The Role of Endothelium in Vascular health

The endothelium is essential to maintain hemostasis and vascular health. The endothelium is an autocrine layer that regulates vasodilation and vasocontraction in response to internal or external stimuli such as blood flow and shear stress. The healthy artery has the ability and the flexibility to dilate in response to shear stress (Kamiya, Ando, Shibata, & Masuda, 1988). The healthy artery has characteristics of anti-coagulant and anti-inflammatory properties. The ability of the artery to dilate in response to shear stress from an increased arterial flow is called Flow Mediated Dilation (FMD). FMD is dependent on the release of the Endothelium-Derived Relaxing Factor (EDRF) such as nitric oxide (NO) which induces relaxation by activation of the endothelium NO synthase(eNOS) (Ignarro, 1989). In contrast, endothelium dysfunction is characterized by the pro-constrictive, pro-coagulant, and pro-inflammatory status of the endothelium. Endothelium dysfunction reduces the generation of NO and increases production of endothelin (ET) which has the constrictive properties. Endothelium dysfunction is an early event in the development of atherosclerotic cardiovascular disease (Fan et al., 2000) and plays a leading cause of cardiovascular disease and stroke (Shechter, Shechter, Koren-Morag, Feinberg, & Hiersch, 2014). Studies have shown that FMD is significantly lower in patients with cardiovascular disease in comparison to a healthy adult. Lower FMD is associated with high cardiovascular event and mortality rate (Uehata et al., 1997). A study showed that a patient with stable cardiac angina who underwent cardiac surgery has a lower FMD in comparison to a patient who did not go to cardiac surgery (Gokce et al., 2003). Different studies targeted the FMD to minimize or prevent potential cardiovascular events by exercise training (Shechter et al., 2014) & (Frederick M. Ivey, Hafer-Macko, Ryan, & MacKo, 2010).

Measuring endothelial function could be attained by assessing FMD in the brachial artery by using a noninvasive ultrasonography technique (Anderson & Mark, 1989). FMD reliability and validity have been established to evaluate endothelium function (Celermajer et al., 1992).

2.3 Role of shear stress to induce Flow- mediated dilation

Endothelial function may be assessed by different chemical agents that lead to endothelium-dependent vasodilation such as acetylcholine (Taddei et al., 1995). In addition to chemical agents, studies show that vasodilatation is derived by Nitric Oxide (NO) bioavailability (Green, Dawson, Groenewoud, Jones, & Thijssen, 2014). Increasing the blood flow, shear stress during exercise contributes to NO synthesis and NO production which lead to dilation (Niebauer & Cooke, 1996). During FMD testing, an occlusion cuff is placed on the upper arm or lower forearm and inflated to supra-systolic pressure (200-220) mmHg for five minutes to block the circulation in the brachial artery. The vasodilation (reactive hyperemia) occurs after an acute increase in blood flow after the deflation of the cuff. That increases the laminar shear forces against the arterial wall. As a result, shear stress is transduced through mechanoreceptors in the endothelial cell. Also, the mechanoreceptors activate G-protein expression of phosphokinase A. This leads to increase signaling of endothelial NO synthase activity which converts L-arginine to NO (Shimokawa et al., 1996). Nitric oxide is a relaxing factor which diffuses into tunica media, then the soluble guanylate cyclase is activated, which convert GTP to GMP to induce smooth muscle relaxation and vasodilation. The percentage of the difference between the arterial diameter before the reactive hyperemia and post the reactive hyperemia is used to calculate the

FMD (Corretti et al., 2002). It is typical for the FMD% to range from 8 to 12% in healthy individuals (Dalli et al., 2002).

2.4 FMD and vascular health and stroke survivors

Disabling stroke causes a metabolic and structural changes in the tissue including the vasculature which alters the circulation (Ryan, Dobrovolny, Smith, Silver, & Macko, 2002). Ivey and her colleagues suggested unilateral impairments vasomotor reactivity after a chronic stroke about 35% in the paretic side in comparison to non-piratic side (Frederick M. Ivey, Gardner, Dobrovolny, & Macko, 2004). Patients with chronic stroke suffer from about a 50% reduction in peripheral hemodynamic and cardiovascular fitness in comparison to similar age-matched individuals (F M Ivey, Macko, Ryan, & Hafer-Macko, 2005). In addition to hemodynamic impairment, FMD and brachial artery diameter is reduced after stroke (Stenborg, Terent, & Lind, 2006)

Exercise training is highly recommended in patients with stroke to improve general health and prevent the prognosis of the disease (S. A. Billinger, Arena, et al., 2014). There is strong evidence of improving vascular function by exercise training within stroke population. For example, Single limb resistance exercises improve the blood flow 35% and femoral artery diameter in patient with chronic stroke (S. A. Billinger, Gajewski, Guo, & Kluding, 2009). In another study, treadmill aerobic exercise training improves the blood flow about 25% in the piratic limb in compassion to control (Frederick M. Ivey et al., 2010). Moderate to high-intensity treadmill aerobic training exercise for eight weeks also improved the FMD in paretic side 18.5%, non-paretic 19.4 % (S. A. Billinger et al., 2012). Moreover, results of a systematic review study showed that high intensity and moderate intensity aerobic exercise improve the vascular function and FMD. However, FMD in the high-intensity aerobic exercise was greater than low-intensity exercise (Ramos, Dalleck, Tjonna, Beetham, & Coombes, 2015).

2.5 Virtual reality video games training in stroke survivors.

The advancement of technology has brought the attention from researchers to develop new rehabilitative interventions as an alternative to traditional physical therapy. Among these alternative interventions is using kinetic video games such as Nintendo Wii and Xbox, which is affordable in rehab sitting for stroke recovery (Saposnik et al., 2010). Also, video games could be a recommended therapy for home exercise programs. In a randomized control trial between virtual reality training by using Nintendo Wii versus conventional physical therapy, a previous study showed that both Wii training and traditional physical therapy improved pain scores, balance, the physical and emotional aspect in patients with chronic stroke (da Silva Ribeiro et al., 2015). The feasibility, safety, and the effectiveness of using virtual Wii training has been achieved to facilitate rehabilitation therapy and promote motor recovery after stroke (Saposnik et al., 2010). Wii virtual training is proven to improve the function of the upper limb, lower limb, balance, and gait in patient with chronic stroke (Laver et al., 2011). Wii Aerobic is a type of aerobic training; a study has shown Wii aerobic training leads to reduction of energy expenditure in patients with chronic stroke and improves the aerobic capacity (Hurkmans, Ribbers, Streur-Kranenburg, Stam, & van den Berg-Emons, 2011).

The effectiveness of virtual Wii training in motor recovery is evident in the literature, but it still unclear if the kinetic Wii training would improve the vascular function, specifically, the FMD, since it plays a key role in vascular health and a strong predictor of a future cardiovascular event or recurrent stroke.

3. Purpose of the study

Endothelial dysfunction serves as an initiating step in the development of cardiovascular disease (CVD), which plays a role in the pathophysiology of stroke (Davignon & Ganz, 2004). FMD is a reliable and valid outcome measurement that evaluates vascular health and predicts future cardiovascular events (Corretti et al., 2002). Patients with chronic stroke suffer from metabolic changes that lead to endothelial dysfunction as well as FMD reduction (Uehara et al., 1997). Exercise training and physical activity are highly recommended to improve the general health, motor function, hemodynamic, and vascular health for patients with chronic stroke (S. A. Billinger, Boyne, Coughenour, Dunning, & Mattlage, 2014). Virtual Kinetic training has been proven as a safe, feasible, and effective alternative therapy in stroke rehabilitation (Saposnik et al., 2010). However, the effect of virtual Kinetic training on vascular health and FMD in patients with chronic stroke has not been discussed yet. Therefore, we have developed a six-week kinetic dance training as a moderate to high-intensity aerobic training, based on heart rate and steps frequency during the intervention, to study the effects of our training on brachial FMD.

3.1 Aim of study:

1) To investigate the effects of kinetic dance training for six weeks on brachial artery FMD in patients with chronic stroke.

2) To compare the effects of our training in patients with chronic stroke to healthy age-matched control.

3.*2Hypothesis*

We hypothesized that 1) six weeks of kinetic dance training with the Xbox video game will improve brachial artery FMD in patients with chronic stroke in comparison to healthy age-matched control group. 2) six weeks of kinetic dance training would lower resting heart, resting blood pressure, and improve blood flow velocity in the brachial artery. Although we have included all outcome measures, our primary outcome measure is the brachial artery FMD.

III. Methods

1. Study population

1.1 Subject selection, recruitment, and characteristics

There are two groups enrolled in the study: the intervention group and healthy age-matched control. **For the intervention group**, participants were recruited from Chicago area hospitals. Flyers were distributed in many buildings at the University of Illinois at Chicago (UIC) and the University of Illinois Hospital. Physician's subjects who met the inclusion criteria were contacted via a sent form to clarify the patients' participation in our study. All participants were asked to sign a consent form to enrolled in the study. Total of eleven subjects with chronic stroke participated in the study at baseline (N=11) male (n=5), female (n=6). There was no age limit, and participants age was between 25-68. Subjects who participated in the Kinetic dance training study had met the inclusion criteria based on the following:

- A clear diagnosis of chronic stroke ≥ six months.
- Functionally independent and able to stand at least 5 minutes without an assistive device.
- Medically stable without any systematic problem.
- No cognition impairment and participants should able to follow instructions. The cognition assessment was done by using Montreal Cognition Assessment Test (MOCA).
- Resting heart rate (HR)< 85.

The healthy age-matched control group was recruited to participate in the study by distributing flyers in UIC buildings, some of them are employees at the UIC. This group did not receive any intervention, but their outcome measures were compared to the intervention group. A total of 8 healthy adults subject (N= 8) were recruited (4 men and four women). All participants completed a written informed consent approved by the UIC IRB. The inclusion criteria were healthy participants who are medically stable. Both groups' participants were reimbursed to each visit. The study protocol and procedures were approved by the UIC IRB.

2. *Outcome* ***measures.***

We collected physical characteristics including age, gender, height, body weight, and BMI. Heart rate and blood pressure were obtained to evaluate the cardiometabolic changes in response to exercise. The vascular parameters were collected as the dependents outcome measurements that we are targeted in our study that includes:

a) Brachial artery diameter at baseline (BSL diameter): the diameter of the brachial artery at baseline before the cuff goes up which represent the standard diameter of the brachial artery.
b) Brachial Artery FMD: the percent of the difference between the brachial artery diameter at baseline and brachial artery diameter after reactive hyperemia.
c) Change in FMD Score: the percent difference of FMD score.
d) Baseline flow velocity (BSL flow): the blood flow velocity at the baseline before the reactive hyperemia.
e) Peak flow velocity: the peak blood flow velocity after the reactive hyperemia.
f) Resting heart rate and BP.
g) Six minutes' walk test (6MWT)

Our primary outcome measure is the %FMD and its change in score. However, we have presented all the outcome measures.

3. FMD protocol

Brachial artery FMD performed according to FMD measuring standards (Corretti et al., 2002). A portable Sonosite brand M-Turbo® ultrasound system was used to evaluate the vascular function according to FMD Testing (Phillips, Das, Wang, Pritchard, & Gutterman, 2011). FMD was done in a temperature controlled room while subjects were lying in the supine position and the paretic arm was abducted 80°-90°. Before the FMD testing, gentle and passive stretching was done by the therapist to overcome the spasticity, the elbow was extended 100°-180°, a second therapist was asked to keep the elbow extended if the spasticity was severe in the paretic arm. Ultrasound images of the brachial artery were performed at a site around one to three centimeters proximal to the antecubital fossa. The ultrasound probe (11 MHz) was perpendicular on the brachial artery to detect superior and inferior lumen-intimal interfaces. Each one-minute video clip for the brachial artery was recorded. At the same site, the flow velocity was measured by taking a picture clip for the flow after ten cardiac cycles. After recording the baseline brachial artery diameter and flow, a BP cuff was placed on the forearm and inflated 50mm Hg above systolic pressure. After five minutes, the BP cuff was deflated to induce shear stress and reactive hyperemia. The brachial artery diameter was recorded continuously for three minutes following the cuff deflation. The peak flow velocity was measured immediately after the cuff deflation with Doppler flow signals. Brachial FMD was calculated as the percent of the averaged value of brachial artery diameter to the averaged value to the largest brachial artery diameter post cuff deflation during the three minutes. Heart rate and blood pressure were measured at baseline, 1 minute, and 3 minutes following cuff deflation.

4. Study design and Data Collection

The study design is a cross-sectional quasi-experimental cohort study with two groups; chronic stroke with kinetic dance intervention, and control healthy age matched. We collect outcome measurements at three-time points for the intervention group; 1) at the baseline before the training, 2) at the end of the second week of training, and 3) after six weeks of training. For the healthy control age-matched group, FMD testing and outcome measures were done only one-time at the baseline. The group did not receive any intervention, but their baseline data were compared to the intervention group at different time points. The primary dependent variable is FMD, and the independent variable is the dance training (Figure 1)

5. Kinetic Dance protocol

5.1 Intervention

The training was kinetic dance based on using Sony Xbox 360 (Just Dance 2014) as high-intensity aerobic exercise. The training protocol was developed by Dr. Bhatt and her colleagues in her previous work (Subramaniam, S., & Bhatt, T., 2015). The training took place in the department of physical therapy at UIC. The training protocol lasted for six weeks and consists of high pace songs and slow pace songs. The fast pace songs are songs that require more steps based on the odometer, whereas the slow pace songs have a fewer number of steps. The Heart rate and the number of steps were measured before and after of each song. The number of weekly sessions and songs per session vary and depends on the week of training.

See scheme 1, scheme 2, table 1

5.2 *<u>Dance frequency and time</u>:*

Week 1-2: The training protocol included five sessions/week. Each session consists of 10 songs (5 slow paces, five fast paces). The total time of the training session was 68.6 minutes that includes (38.6 minutes of dance + 10 minutes stretching + 20 minutes for rest interval). The average time for each song is 3.79 minutes. There was an optional two minutes rest period between each song if the participant feels he/she could continue at HR <85 bpm. Heart rate and pulse were recorded immediately after each song to make sure that the heart rate of the 60-90% of maximum heart rate.

Week 3-4: The training consists of 3 sessions per week every other day. The protocol is similar to week 1-2, but we added two songs (one fast, one slow). The total time of dance is 45.5 minutes+ 2 minutes resting interval after each song+ 10 minutes stretching before and after.

Week 5-6: The training protocol is two sessions/week. In week five there are two days off during the intersession period which progressed to 5 sessions at week six. The training protocol is similar to week 3-week 4, with the inclusion of two songs (one fast, one slow). The total time of dance is 52.42 minutes+ 2 minutes resting interval after each song+ 10 minutes stretching before and after.

See Table 2 for the time of training, scheme 2, scheme 1.

5.3 *<u>Preparation.</u>*

We measured Heart Rate and BP before starting the session. In the beginning, participants were instructed performing a 10-minute warm-up stretching exercises before and after playing the game to reduce the risk of exercise-related adverse effects. Participants were asked to mimic the movements as much as possible, and the system will give a feedback and scoring points about the accuracy of mimicking the dance. Before starting the session, we confirmed that the system could detect the participant's movement.

6. Statistical analysis

All data represents mean ±standard deviation, and we used IBM SPSS 23 for the statistical analysis. Repeated measures ANOVA were utilized in the chronic stroke group to test the effect of dance training on FMD at baseline, week2, and post. The significant level is ($P \leq 0.05$), and Bonferroni correction was used to reduce the error. We used the pairwise comparison to locate the significance of the time of training. Six subjects (N=6) were included in the statistical analysis repeated measure ANNOVA. Four participants missed the FMD testing at the mid-point testing visit. In post testing eight subjects completed the trial, one subject did not complete the testing, and two subjects were excluded from the statistical analysis because of technical difficulties. Additionally, independent T-test was used to include more participants in the statistical analysis to compare the effect of post-training to baseline, the significant level is ($P \leq 0.05$).

For the FMD analysis, we used the software Brachial Analyzer for Research from the company Medical Imaging Application LLC to analyze the brachial artery diameter and flow velocity. We averaged the brachial artery diameter for 10 seconds (75 frames) before and after reactive hyperemia. Microsoft Office Excel software 360 were used to calculate the FMD according to the following formula:

FMD %= (peak diameter- baseline diameter)/ (baseline diameter) *100. SPSS was used to statistical analysis whereas Microsoft Excel was used to create graphs.

IV. Results

1. Demographics

At the baseline, the total of 11 patients with chronic stroke involved in the dance training (N=11; male n=5; female n=6) average age was 58.82 ±11.83, and BMI 29.03± 4.31. Because of technical difficulties, eight subjects out of 11 were included in the statistical analysis at week six, whereas six participants were included in midpoint analysis. **For the age-matched control group**, eight subjects were included (Male n=4, female n=4). We missed measuring the resting flow velocity data for five subjects, but we included only three subjects for resting flow velocity. The average age of the control group was 60± 4.56 and BMI was 30.45 ± 9. 25. See Table2

2. **Outcome measures at baseline Chronic Stroke Vs Age-Matched**

2.1 FMD and baseline brachial artery diameter.

There was no significant difference between baseline brachial artery diameter between chronic stroke and control groups (4.03±.0.94, 4.09±0.65), respectively, (P=.809). FMD was significantly lower (P= 0.01) at the baseline in the stroke group (n=11) (5.81%±1.62) comparing to the healthy group FMD (7.62%± 1.65). Groups were homogeneous, and variances were not significantly different (P=0.66) for Levene's test. The effect size had a large effect (r^2=0.7). FMD in the chronic stroke group was 31.1% lower than the healthy age-matched adults. See Table 2, Figure3.

2.2 Heart rate, BP, and Flow data:

Before the dance training, heart rate was significantly lower (P=0.016) in healthy age-matched control (n=8) (70.43 ±10.35) compared to chronic stroke (n=11) (84±9.7). Homogeneity was achieved between groups p=0.54, and the effect size was (r^2=0.63). Systolic and Diastolic BP was lower in the age-matched group but was not significantly different (p=0.86), (P=0.54) respectively. There was no significant difference in the flow after reactive hyperemia between the chronic and healthy control. See Table 2.

3. Outcome measures after Dance Training for the stroke group.

3.1 FMD ***and brachial diameter.***

The FMD significantly improved at week2 (%6.85±1.3) (p=0.017) and week six (%7.92±2.06) (p=0.025) after training comparing to baseline (5.96±0.78). Data were normally distributed (P=0.47), effect size was 67%($n^2 = 0.67$). FMD was not difference at week two to week six (p=1.04) (figure 4, table 3). Brachial artery diameter was not different six weeks of training (4.25±.87) from baseline (4.02±.91) p=0.2, and at week two of the training (4.1±.91) (P=0.76) (Table3). Six weeks of kinetic dance training has improved the FMD score (14.9 %) after two weeks of training, and (32.88%) after six weeks of training. See figure 5.

3.2Heart rate, BP, flow velocity and 6MWT.

There was a general reduction in systolic BP, and diastole BP, but there were not significantly different. Heart rate reduced significantly at week 6 (73.50±2.1), and week2 (74.20±1.4) comparing to baseline (84±9.7) (p=0.01, 0.007), respectively. The effect size was 51% $n^2 = 0.51$, and data normally distributed p=0.45. Reactive hyperemic flow velocity didn't change significantly with repeated measures analysis although there is a trend of improvement after training. See Table 3. Independent pre-post t-test was done to increase the sample size(n=8). FMD, resting flow velocity, and heart rate were significantly improved from baseline. (See Table 4, figuer6, Figure 7). 6MWT did not change significantly at week 6 (422.80±83.43), p=0.15 and week2 (409.40±92.12) p= 1.0 comparing to baseline (407.50±87.10).

4. Outcome measures post training: Age-matched vs. chronic stroke

4.1 *FMD and Brachial artery diameter*

FMD after six weeks of dance training for chronic stroke (7.92±2.06) was not significantly different (p =0.81) to the healthy age-matched control group (7.62±1.65). Similarly, FMD was not significantly different at week 2 of training (%6.85±1.3) comparing to control. The only significant different was between control (7.62±1.65) and stroke (5.81%±1.62) at the baseline (P=0.001). FMD improved in chronic stroke group 32.88% following six weeks of dance training. See figure 8.

V. Discussion and conclusion

To the best of our knowledge, this is the first study investigating the effect of Virtual kinetic dance training after the chronic stroke on the brachial artery FMD. Stroke survivors have reduced blood flow in the paretic side (35%) and nonpractice side (32%) due reduction in metabolic demands which leads to a reduction in vascular flow and arterial diameter (Frederick M. Ivey et al., 2004). This decrease because of physical inactivity, therefore, few metabolic demands occur after chronic stroke. (Landin, Hagenfeldt, Saltin, & Wahren, 1977). Our finding revealed 31.1% reduction of FMD compared to healthy age-matched which is expected because of impaired endothelium function the following stroke as prescribed by (Stenborg et al., 2006). This impairment could be altered by prescribing proper exercise to improve hemodynamic and blood flow. Billinger and her colleagues suggest that single limb resistance training would improve the femoral blood flow, diameter, peak velocity and vascular conductance (S. A. Billinger et al., 2009). They concluded that single limb exercise improves femoral artery blood flow 41% on the paretic side, whereas only 4.37% remains deficit in paretic comparing to non-paretic limb following four weeks of single resistance exercise. Their finding illustrates that exercise leads to vascular remodeling as prescribed in literature (Miyachi et al., 2001). Also, in another study, Billinger and her colleagues found 18.5% improvement in brachial artery FMD in subacute stroke patients after four weeks of aerobic recumbent treadmill training (S. a Billinger et al., 2012).

We hypothesized that six weeks of kinetics dance training would improve the brachial artery FMD after chronic stroke. Our results showed that aerobic kinetic dance improves the brachial artery FMD 14.98% after two weeks of training, and 32.88% after six weeks of training. Also, the resting flow velocity has improved 40% after six weeks of training. Our finding supports previous work by Billinger and her colleagues, however, using video gaming for the purpose of improving the brachial artery FMD is what we have achieved. This finding supports the hypothesis of vascular adaptation to exercise after aerobic training (Macko et al., 1997). Although we did not investigate the underlying mechanism of the improvement, a possible explanation is an effect of exercise on endothelial function and NO bioavailability.

Potential mechanisms

Endothelium function and vasodilatation are dependents in releasing relaxing factor such as NO and reduction in Oxidative stress. Increasing the shear stress resulting from high arterial flow during exercise training leads to improving the signaling from endothelium and NO bioavailability. The mechanic- receptors in the endothelium detects the shear stress which activates eNOS by converting L-arginine to NO. NO diffuses to smooth muscle to induce relaxation. Therefore, Kinetic dance training could improve the vascular function and FMD throughout improving NO bioavailability.

Limitation

We have concluded our finding from small sample size 11 subjects, and we included only eight subjects in the repeated measures analysis, indeed, restricted us to draw a conclusion about the effect of our training on hemodynamics following the chronic stroke. Also, our methods did not control the factors that might affect the FMD testing such as fasting from food before the FMD testing and diet. Additionally, not all subjects completed the flow analysis, therefore, the effect of our training on flow and hemodynamics is limited. Our training did not improve 6MWT significantly after six weeks of training. However, small sample size could limit us from drawing a significant result taking in consideration there was a general improvement in 6MWT score after training. Future studies should address the effect of our training on both paretic vs. none paretic in a randomize control design, and including functional outcome measures.

Conclusion

FMD is significantly impaired in chronic stroke compared to healthy age-matched adults. Kinetic dance training improves the vascular function by improving the brachial artery FMD in chronic stroke14.9 % after two weeks of training, and 32.8 % after six weeks. Our Kinetic dance training could be considered in stroke rehabilitation to improve vascular function and FMD following chronic stroke.

List of Tables

I. Table 1. Dosage and Frequency for the dance Kinetic Training

Week	Time of dance (mins)	Session/week	Rest intervals
week1-2	38.6	5 sessions/week	Pre-stretching (10 min.) + resting intervals (5 min.)
Week 3-4	45.5	3 sessions/week	Pre-stretching (10 min.) + resting intervals(5min)
Week4-6	52.42	2 sessions/week	Pre-stretching (10 min.) + resting intervals (5 min.)

Table 1: Dance frequency and time of exercise during the study at every week. The time of exercise is gradually increased. Subjects had 10 mins stretching exercise and 5 mins resting intervals between songs if needed.

II. Table2: Demographics and outcomes for the control and stroke groups at baseline.

	Chronic Stroke (N=11)	**Healthy Age-Matched (N=8)**
Age (year)	58.82 ±11.83	60± 4.56
Year of onset (year)	10.6±5.4	---
Gender	Male n=5, female n=6	Male n=4, Female n=4
BMI (kg/m²)	29.03± 4.31	30.45 ± 9.25
BSL diameter (mm)	4.03±.0.88	4.09±0.65
FMD %	5.81%±1.62	7.62± 1.65*
Baseline Flow velocity (cm/s)	54±7.02	72.16±10.12 (n=3)
Reactive hyperemic flow velocity(cm/s)	100.81±23.016	95 ±9.23(n=3)
Systole	130.00±6.34	127.71±5.61
Diastole	87.00±10.78	81.38±9.36
Pulse	84±9.7	70.43±10.35*

Table2: Demographics and physical **characteristics** of chronic stroke and healthy age-matched group at baseline before the dance training. (*, P $\leq$ 0.05). Data are presented as Mean ± SD

III. Table3: Outcome Measure After Kinetic Dance Training in Patients with Chronic Stroke(n=6)

Outcome	**Baseline**	**Week2**	**post**
Baseline diameter(mm)	4.02±.91	4.1±.91	4.25±.87
Baseline flow velocity (cm/s)	54±7.02	61.8±5.21	64.11±8.21
Peak Flow velocity (cm/s)	96.72±21	106.6±28	111.40±15.56
FMD (%)	5.96±0.78	6.85±1.3*	7.92±2.06*
Absolute change in FMD scores (%)		14.9%	32.88%
Systolic BP (mmHg)	128.27±11.951	121.64±9.64	123..27±3.66
Diastolic BP (mmHg)	85.45±17.68	89.64±13.67	82±9.52
HR (bpm)	84±9.7	74±4.38*	74.09±6.73*
6MWT	407.50±87.10	409.40±92.12	422.80±83.4

Outcome measures after training for six patients with chronic stroke. Results are compared to baseline (*, $P \leq 0.05$).

IV. Table4: Outcome measures at baseline and after six week of dance training (Pre- post)

Outcome	Pre(n=8)	Post(n=8)	P Value
Systolic BP (mmHg)	127.40±10.16	123.78±3.866	0.3
Diastolic BP (mmHg)	85.45±17.683	82.20±10.020	0.61
HR (bpm)	84.00±9.726	73.50±6.786	*0.010
6MWT	379.45±124.42	418±80.73	0.39
Baseline Diameter (mm)	3.67±0.86	4.08±1.02	0.39
BSL Flow velocity (cm/s)	55.83±6.96	80.25±30.89	*0.046
Reactive hyperemic Flow (cm/s)	83.33±13.63	101.94±22.96	0.18
FMD Diameter mm	3.80±0.80	4.43±1.14	0.22
FMD%	5.76±0.78	7.83±1.17	*0.001

Table 4: Outcome measures for eight subjects with chronic stroke at baseline and after six-week post dance training. (* P≤0.05)

List of Graphs

I. Figure1. Number and distribution training sessions

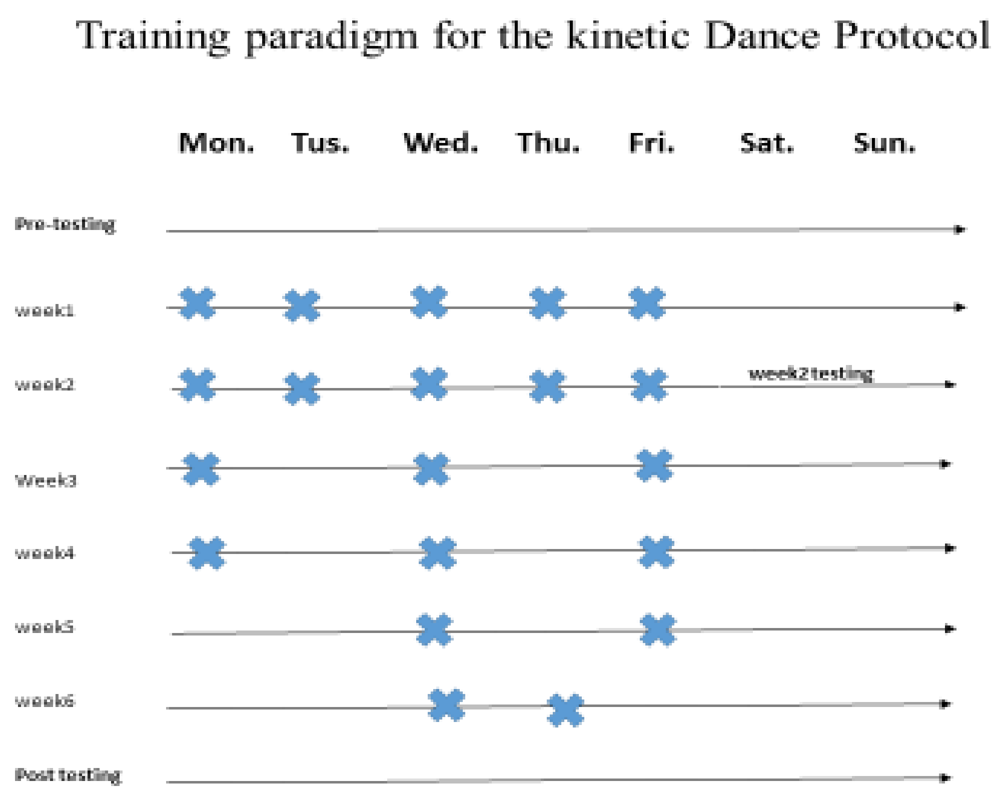

Figure1: number and distribution of the dance training sessions in every week for the intervention group.

II. Figure2: weekly dance protocol.

Dance Training Paradigm for The Kinetic Dance

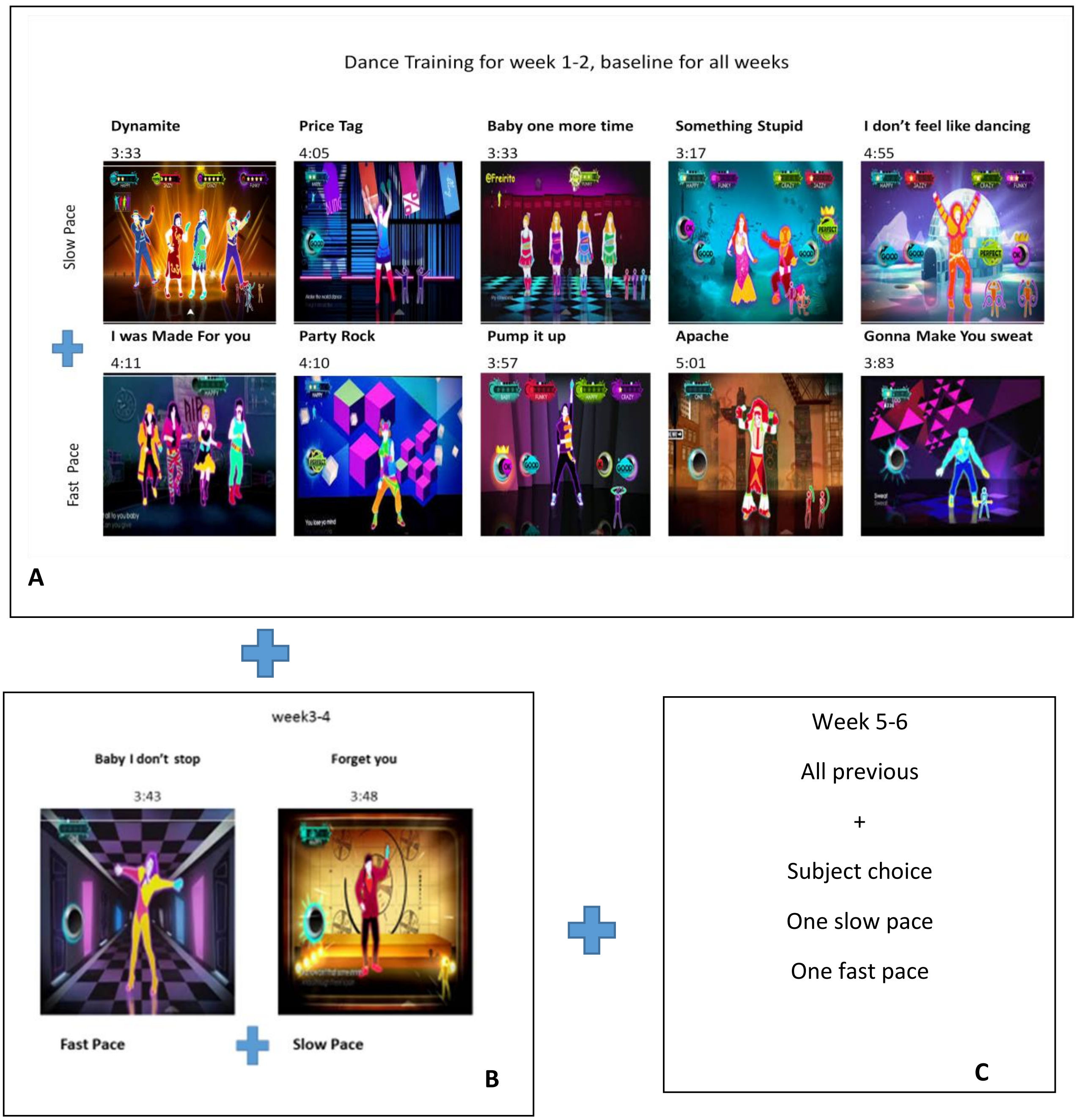

Figure 2: Dance kinetic training protocol for the patients with chronic stroke at week 1-2 (A), week 2-3 (A+B), and week 5-6 (A+B+C)

III. Figure3: baseline brachial artery diameter and FMD (stroke and control)

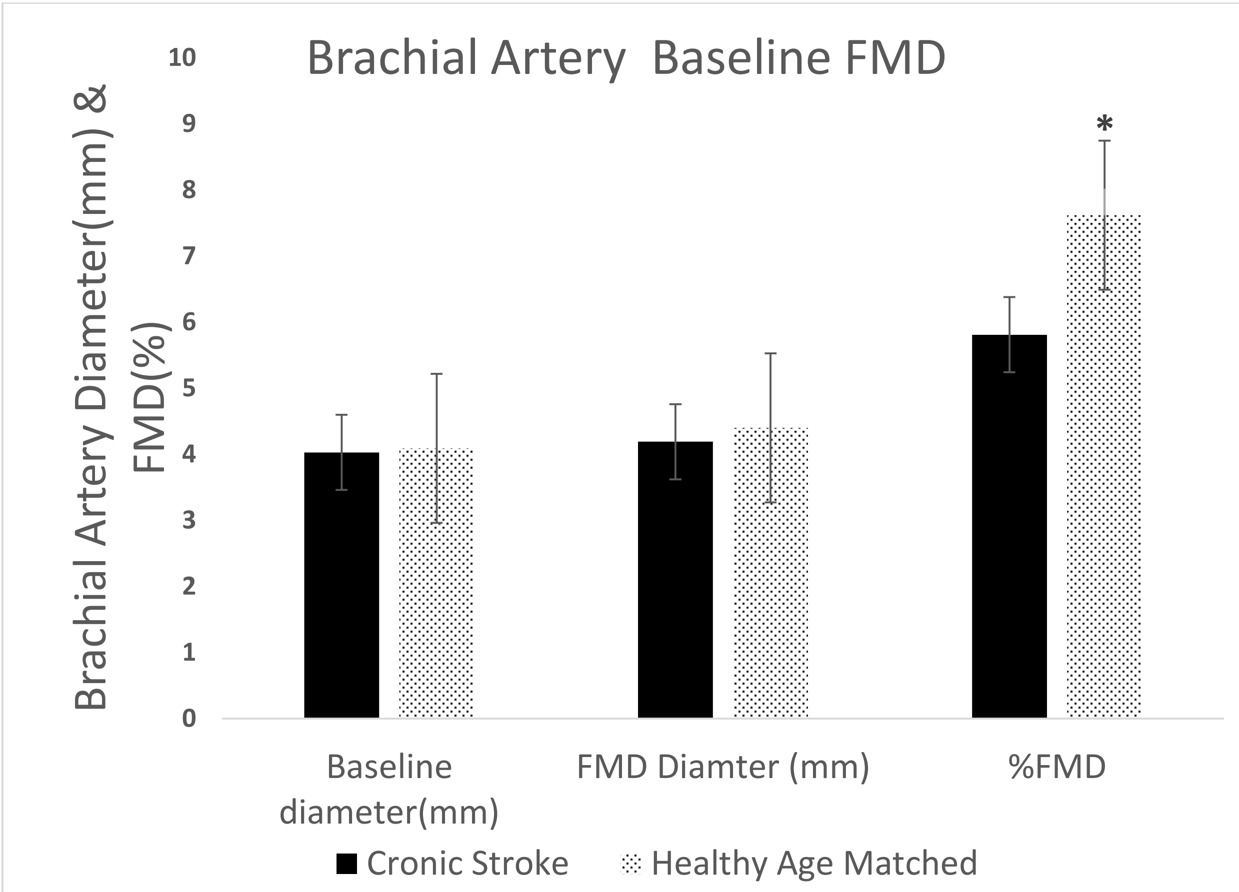

Figure 3: FMD and brachial artery diameter at baseline before and after reactive hyperemia between chronic stork (n=11) (black filling) and age-matched control (n=8) (patterned filling). FMD is significantly different between groups at the baseline. (*, $P \leq 0.05$)

IV. Figure 4: Effect of Kinetic Dance Training in FMD in Chronic Patients with Stroke

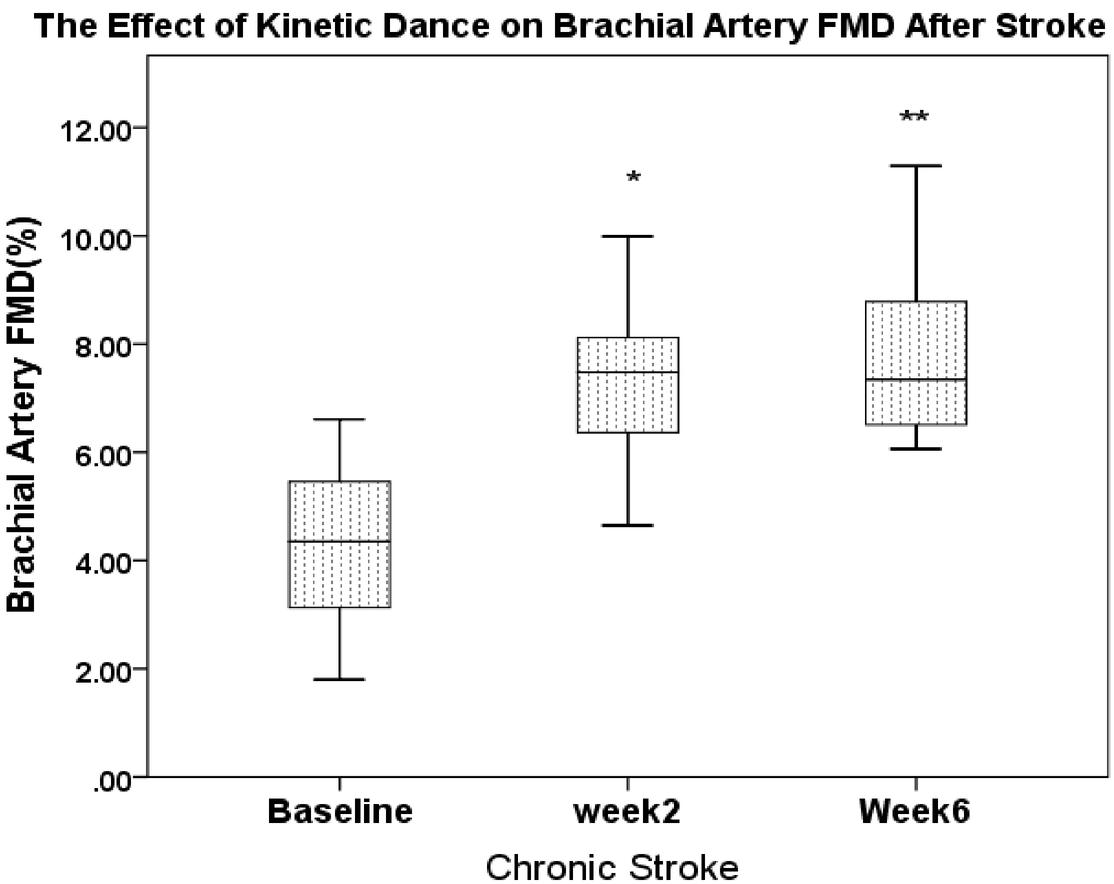

Figure4: FMD after Kinetic dance training is (6.85±1.3) at week 2, and (7.92±2.06) at week six, and is significantly different from FMD at baseline (5.96±0.78) after chronic stroke N=6. (*, **, $P \leq 0.05$)

V. Figure 5. Changing in FMD score from baseline.

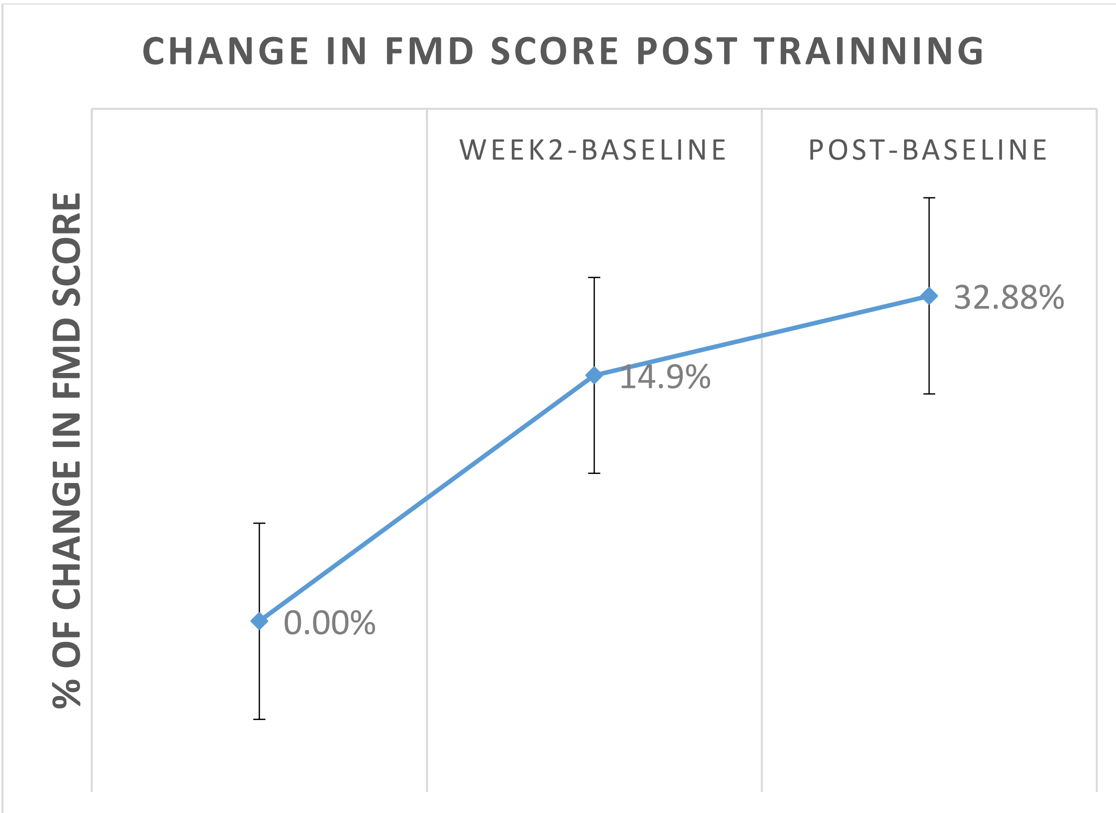

Figure 5: Kinetic Dance training patients improves the FMD for 14.9 % after two weeks of training, and 32.88% after six weeks of training in patients with chronic stroke (n=6).

VI. Figure6: HR and BP After Six Weeks of Dance Training.

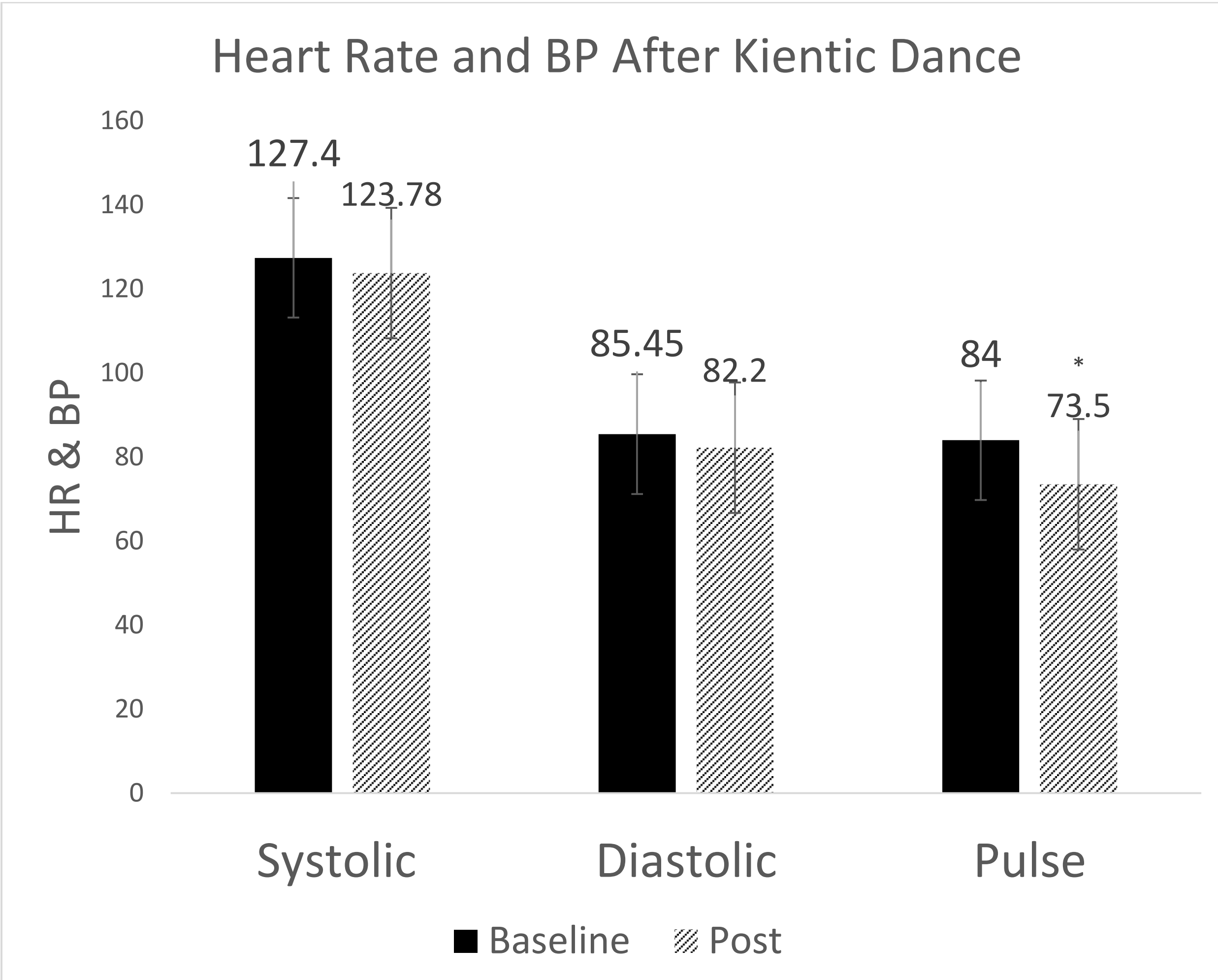

Figure 6: The effect of six weeks of dance training on BP and Heart Rate in patients with chronic stroke at baseline and after 6 weeks of training (n=8), (*, P≤0.05).

IX. Figure7: Baseline and Hyperemic Flow After six weeks of Dance training

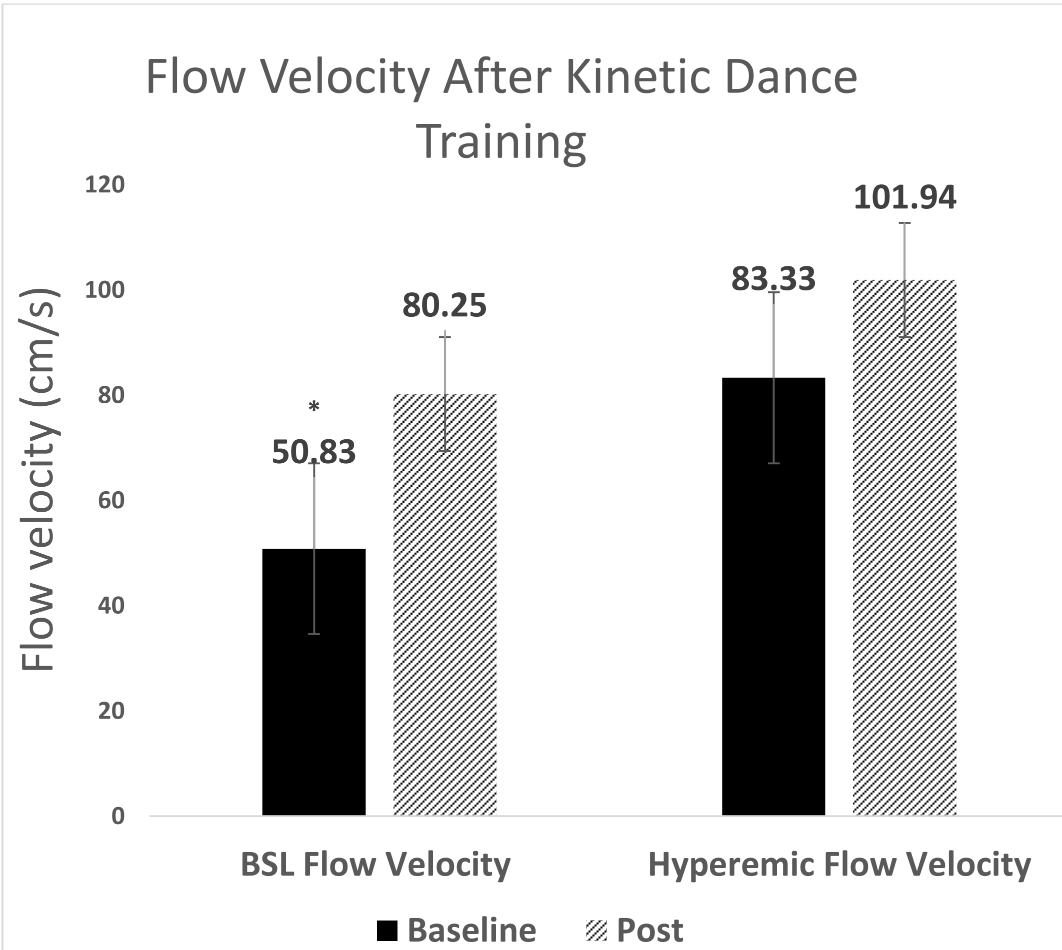

Figure 7: Baseline and hyperemic flow for eight subjects with chronic stroke after six weeks of kinetic dance training (*, P≤0.05).

X. Figure 8: Brachial Artery FMD post training comparing to Age-Matched

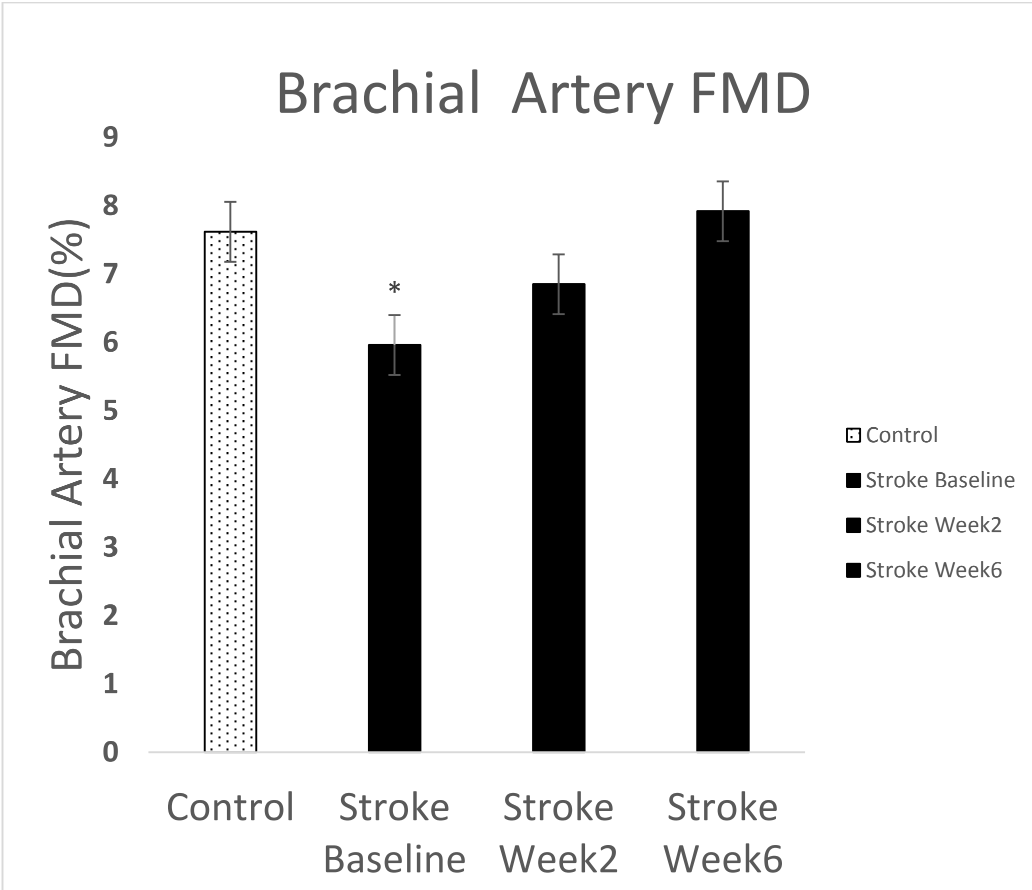

Figure 8: Brachial artery FMD in patients with chronic stroke (Solid filling) was only significant lower at baseline before the dance training in comparison to age-matched control(patterned). (*P≤0.05)

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