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LOMA LINDA UNIVERSITY
School of Allied Health Professions
in conjunction with the
Faculty of Graduate Studies

The Effect of Cervical Muscle Fatigue on Postural Stability during
Immersion Virtual Reality

by

Mazen M. Alqahtani

A Dissertation submitted in partial satisfaction of
the requirements for the degree
Doctor of Science in Physical Therapy

June 2015

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Each person whose signature appears below certifies that this dissertation in his/her opinion is adequate, in scope and quality, as a dissertation for the degree Doctor of Philosophy.

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LIST OF PUBLICATIONS

This present work is based on the following papers, which are referred to in the text by their roman numerals;

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CONTENT

Approval Page.....	iii
Acknowledgements.....	iv
List of Figures.....	ix
List of Tables.....	x
List of Abbreviations.....	xi
Abstract.....	xii
Chapter	
1. Introduction.....	1
Understanding of Postural Stability.....	1
Irregular Cervical Somatosensory Input.....	1
Neck Muscle Fatigue and Somatosensory.....	2
Neck Muscle Fatigue and Postural Stability.....	2
Visual system and Postural stability.....	2
Sensory Organization Test.....	3
Motion Sensitivity.....	5
Summary.....	6
2. The Effects of Neck Muscle Fatigue on Postural Stability During Immersion Virtual Reality.....	7
Introduction.....	9
Methods.....	13
Participants.....	13
Sample Size.....	13
Randomization.....	13
Study Design.....	14
Data Collection and Balance Assessment.....	14
Neck Fatiguing Protocol and Experimental Procedure.....	19
The Cervical Spine Isometric Contraction Protocol.....	21
Sham Exercise Protocol.....	23
Data Analysis.....	23
Result.....	24
EMG Findings.....	24
Main Findings.....	32
Discussion.....	39

Conclusion	42
Acknowledgment	42
References.....	43
3. General Discussion	47
References.....	43
Appendices.....	43
1. Self-Report Questionnaire	54
2. Informed Consent Form.....	55

TABLES

Tables	Page
1. The mean load weight of experimental group	28
2. The mean median frequency of experimental group	29
3. Experimental group EMG level of change	30
4. The mean amplitude of experimental group	31
5. Baseline characteristics of subjects.....	33
6. SOT1 within and between groups.....	34
7. SOT4 within and between groups.....	35

FIGURES

Figures	Page
1. Bertec Balance Advantage-Dynamic CDP	16
2. A continual visual flow	17
3. Consort flowchart diagram	18
4. Dorsal neck EMG electrodes	20
5. A customized neck exercise machine	22
6. Median Bower Frequency in experimental subjects	26
7. Amplitude in experimental subjects.....	27
8. SOT 4 means between groups.....	36
9. SOT1 means between groups.....	37
10. Over all SOTs between groups	38

ABBREVIATIONS

AMP	Amplitude
CCN	Central cervical nucleus
CDP-IVR	Computerized dynamic posturography with immersion virtual reality
CGD	Cervicogenic Dizziness
EMG	Electromyography
JPE	Joint Position Error
MPF	Median power frequency
mVAS	Modified Visual Analog Scale
MVC	Maximum voluntary contraction
SOT	Sensory organization test
SOT1	Sensory organization test condition 1
SOT4	Sensory organization test condition 4
VOR	Vestibulo-Ocular reflex
COR	Cervico-ocular reflex
CSR	Cervico-spinal reflex
VSR	Vestibule-spinal reflex
VBI	Vertebrobasilar insufficiency
WAD	Whiplash-associated disorder

ABSTRACT OF THE DISSERTATION

The Effect of Cervical Muscle Fatigue on Postural Stability during Immersion Virtual Reality

by

Mazen M. Alqahtani

Doctor of Science, Graduate Program in Physical Therapy

Loma Linda University, June 2015

Dr. Eric Johnson, Chairperson

The visual system is part of the nervous system that enables an individual to scan their environment and assess distance to and from objects. The information captured from our navigating environment is communicated to the brain, which in turn makes the decision on how we respond to spatial orientation. This is particularly useful in helping with balance and determining direction of movement. Our posture and visual stability rely heavily on an efficient and processing of visual, vestibular, and proprioception afferent input. Erroneous sensory information from defective sensory organs may cause a person to experience feelings of lightheadedness, spinning and whirling sensations, and difficulty in maintaining straight posture. Few studies have examined the synergy between cervical spine proprioception and the vestibular ocular reflex (VOR) and as such, their impact on human VOR is less understood. The purpose of this study therefore was to investigate how motion sensitivity is impacted by neck muscle fatigue in normal healthy participants.

The overall aim of the present work was to investigate whether impaired somatosensory information from the cervical spine, caused by neck muscle fatigue, would negatively impact postural stability in healthy young participants. Results indicated that healthy young participants who were fatigued had significantly poorer postural stability than

those who were not fatigued ($p < 0.001$).

In Conclusion, our research suggests that when assessing motion sensitivity in patients complaining of dizziness with a history of neck trauma, one may consider that VOR dysfunction could have a cervical origin due to somatosensory disturbance, which may lead to poor postural stability.

CHAPTER ONE

INTRODUCTION AND REVIEW OF THE LITERATURE

Understanding Postural Stability

Balance, or postural stability, is maintained through a cooperative interaction of sensory inputs and efferent outputs [16]. Whitney described postural stability as sensorimotor activity causing the body's center of gravity to steady itself in response to self-initiated or external stimuli [32]. The body orients itself using extraneous fixed cues such as a wall to interpret movement as its own [37]. Postural stability is achieved through an interaction of visual, vestibular, and somatosensory systems [15].

Irregular Cervical Somatosensory Input

Postural instability can be caused by numerous factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma. Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [3,11,13,14,21-24]. The cells emerging from the C2 dorsal root ganglion innervate the upper cervical spine and gather in the central cervical nucleus (CCN) [6,9]. The CCN functions as a passageway to the cerebellum which is responsible for coordinating and harmonizing vestibular, ocular, and proprioceptive information relative to the head, neck and body [2,6,9,12]. Interruption in this passageway can result in dizziness, unsteadiness and visual disturbance [9,32]. Furthermore, evidence suggests that impairments in the discharge of sensory receptors in the upper cervical spine negatively effects proprioception of the head and neck [6,12,19].

Neck Muscle Fatigue and Somatosensory

Stapley et al [28] observed increased postural sway in subjects with cervical spine whiplash injuries after fatiguing their dorsal neck muscles. Isometric dorsal exercise was performed on the patients for 5 minute. Postural stability was measured before and after the exercise using a dynamometric force platform. Also, electromyography (EMG) was used to determine the neck muscle fatigue for all subjects. Following the exercise, 7 subjects out of 13 subjects showed signs of fatigue and increased postural sway suggesting a connection between neck muscle fatigue and impaired postural stability. The 6 subjects that did not reach fatigue did not demonstrate increased postural sway.

Neck Muscle Fatigue and Postural Control

Vuillerme et al [25] investigated the effects of cervical muscular fatigue on postural control under multiple sensory conditions. Their results showed that cervical muscle fatigue exacerbated center of foot pressure displacement in the absence of vision. The authors suggested that there is a correlation between neck muscle fatigue and impaired postural stability.

Visual System and Postural Balance

The visual aspect is an important component of the systems. Several studies have examined vision and its role on postural stability [5,34]. Although difficult to isolate, visual input may act synergistically with the vestibular and somatosensory systems. Dynamic visual motion detected by the retina (visual background) may result in either self-motion or environment-motion sense [10,15]. Many studies have examined the effect of dynamic visual motion (rotate or create a tunnel visual scene effect) on postural

stability [7,36]. Peterka and Benolken [30] reported no differences in postural stability amplitude between healthy subjects and subjects with vestibular loss, both groups were subjected to a sinusoidal black and white moving scene. The investigators suggested that the somatosensory system in subjects with vestibular loss did not compensate for their vestibular deficit. Also, they suggested that the threshold for the somatosensory cues in healthy subject were greater compared to vestibular cues [30]. Moreover, Borger and colleagues [18] examined the influence of dynamic visual environments on postural stability in older adults. Using a computerized dynamic posturography (CDP) platform, 10 young and 10 older healthy subjects participated in the study. For 3 days a total of six experimental trials were given to each subject. All subjects were exposed to a dynamic sinusoidal black and white moving scene with eyes open for 30 seconds of quiet stance and another 60 seconds of actual scene movement. Results showed that older subjects are more influenced by dynamic visual information for postural stability than young adults [18].

Sensory Organization Test

The sensory organization test (SOT) is a tool that helps clinicians determine the affected sensory systems that contribute to postural stability. Based on the findings, clinicians can provide the proper interventions for patients. The SOT is composed of six sensory conditions: (1) normal vision with fixed support (baseline for eyes open); (2) absent vision with fixed support (baseline for eyes closed); (3) swayed-reference vision with fixed support; (4) normal vision with swayed-referenced support; (5) swayed-reference support with absent vision; and (6) swayed-referenced vision with swayed-

referenced support. In this study, investigators assessed subjects' postural stability during quiet and dynamic stance using the Bertec Balance Advantage-Dynamic CDP. Two consecutive measures of sensory organization test (SOT) condition 1 and 4, (1) normal vision with fixed support and (4) normal vision with sway-referenced support, with a continual visual flow that was independent of the subjects' movements were performed. Using a computer, signals from the subjects' effort to maintain balance was sampled and analyzed at 1000 Hz following and sway path was computed. SOT scores use a Sway Area calculation sway path with equilibrium score quantified how well the subjects sway remains within the expected angular limits of stability during each SOT condition. The following formula was used to calculate the equilibrium score:

$$\text{Equilibrium Score ES} = ([12.5\text{deg} - (\text{the taMAX} - \text{the taMIN})] / 12.5\text{deg}) * 100$$

12.5 degrees is the normal limit of the AP sway angle range. Subjects exhibiting little sway will achieve equilibrium scores near 100, while subjects approaching their limits of stability will achieve scores near zero. The Bertec Balance Advantage-Dynamic CDP calculated the Equilibrium Score based on Sway Angle, which does compensate for a person's height.

The following formula was used to calculate the sway angle:

$$\text{Sway Angle} = \arcsin (\text{COGy}/(.55*h))$$

The inverse Sin of the center of gravity would be divided by 55% of a person's height. The age of subject was not factored into the calculation, however the normative values for the SOT are based on different age ranges 20-49, 50-59, 60-69, and 70-79. Additionally, the optokinetic flow used in the continual visual flow was in thicker lines and with highest degree per second the velocity determined to challenge subject visual

perception.

Motion Sensitivity

Motion sensitivity is a condition characterized by dizziness resulting from full field repetitive or moving visual environments of visual patterns. Many arguments exist as to the root cause of motion sensitivity. One such argument attributes motion sensitivity to a discord between the visual, vestibular, and somatosensory systems; hence likelihood exists of dissimilarity between what a person anticipated and the actual extraneous stimuli a person received. Another argument suggests that visual vertigo is a composite of vestibular disorder and subsequent visual dependence. Others have also suggested that too much reliance on visual cues for sight and posture control restricts vestibular compensation resulting in visual-vestibular clash, hence motion sensitivity.¹⁴ This view is supported by among others, findings that vertical perception and postural stability of patients with vestibular dysfunction and motion sensitivity is influenced by disorienting visual stimuli (tilted or rotating visual surroundings) compared to those without¹⁴.

Guerraz et al⁴ recommends optokinetic stimulation (OKS) therapy for patients with VV with the sole purpose of desensitization and increasing visual motion tolerance. A Study examining this theorem found that patients with chronic peripheral vestibular dysfunction profited more from customized vestibular rehabilitation incorporating OKS exposure by means of whole body or visual environment rotators resulting in improved dizziness, postural instability, and more so improvement in motion sensitivity symptoms⁵.

Nonetheless, it must be mentioned that visual dependency was not measured and therefore definite recovery mechanisms remain unknown. We therefore speculate that patients with motion sensitivity undergoing visuo-vestibular rehabilitation experience an

improvement in symptoms of motion sensitivity by way of plastic, adaptive changes in visual dependency magnitude. However, whether it is plastic or not remains unexplained. An investigation to this effect was conducted in this study where visual dependency in healthy subjects was measured at both, perceptual and postural levels, before and after repeated OKS exposure.

Summary

In summary, Postural stability is achieved through an interaction of visual, vestibular, and somatosensory systems. The visual aspect is crucial critical component of the systems. Many studies have examined vision and its role on postural stability. Also, visual input may act synergistically with vestibular and somatosensory systems. On other hand, Postural instability can be caused by many factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma. Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [3,11,13,14,21-23]. Postural instability can be caused by many factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma. Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [3,11,13,14,21-23]. Given the lack of empirical evidence, the interaction between cervical spine proprioception and the VOR and its impact on humans is not well understood [12,25,30]. We studied the effect of neck muscle fatigue on healthy subjects exposed to visual stimuli and compare it with subjects exposed to visual stimuli without neck muscle fatigue.

CHAPTER TWO
THE EFFECT OF CERVICAL MUSCLE FATIGUE ON POSTURAL
STABILITY DURING IMMERSION VIRTUAL REALITY

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0459; E-mail: ejohnson@llu.edu.

Abstract

The purpose of this study was to investigate the effect of dorsal neck muscle fatigue on postural stability during immersion virtual reality. Postural stability was measured in 41 healthy male subjects ages 20-39 using computerized dynamic posturography with immersion virtual reality (CDP-IVR). Twenty-one subjects were randomly assigned to the experimental group and 20 subjects to the control group. Fourteen of 21 experimental group subjects reached neck muscle fatigue after 5 minute of isometric dorsal neck muscle contractions. The amplitude and median power frequency of neck muscle EMG were recorded for the contraction period to determine the muscle fatigue. Pre-assessment between groups showed no significant differences in postural stability for both CDP-IVR testing conditions (stable and unstable support) ($p=0.182$, $p=0.158$). Post-assessment between groups showed significant differences in postural stability for both conditions ($p<0.001$). Our findings suggest that dorsal neck muscle fatigue decreases postural stability during immersion virtual reality.

Keywords: Postural stability, immersion virtual reality, sensory organization test, motor learning.

Introduction

Balance, or postural stability, is maintained through a cooperative interaction of sensory inputs and efferent outputs [18]. Whitney et al [35] described postural stability as sensorimotor activity causing the body's center of gravity to steady itself in response to self-initiated or external stimuli. The body orients itself using extraneous fixed cues such as a wall to interpret movement as its own [14]. Postural stability is achieved through an interaction of visual, vestibular, and somatosensory systems [28].

Postural instability can be caused by numerous factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma. Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [9,10,12,23-25,31]. The cells emerging from the C2 dorsal root ganglion innervate the upper cervical spine and gather in the central cervical nucleus (CCN) [5,15]. The CCN functions as a passageway to the cerebellum which is responsible for coordinating and harmonizing vestibular, ocular, and proprioceptive information relative to the head, neck and body [5,6,13,15]. Interruption in this passageway can result in dizziness, unsteadiness and visual disturbance [5,27]. Furthermore, evidence suggests that impairments in the discharge of sensory receptors in the upper cervical spine negatively effects proprioception of the head and neck [1,13,15]. Visual input is an important component of postural stability [16,21]. In particular, dynamic visual motion, such as projected visual scenes, can result in the perception of self or environment movement and cause postural instability [8,17,28,33]. Peterka and Benolken [22] reported no differences in postural stability amplitude between healthy subjects and subjects with vestibular loss when subjected to a sinusoidal black and white

moving scene. The investigators suggested that the somatosensory system in subjects with vestibular loss did not compensate for their vestibular deficit. Also, they suggested that the threshold for the somatosensory cues in healthy subject were greater compared to vestibular cues. Moreover, Borger et al [3] examined the influence of dynamic visual environments on postural stability in older adults. Subjects were exposed to a sinusoidal black and white moving scene and an actual moving scene. Results showed that postural stability in older subjects was more influenced by dynamic visual information compared.

Pinsault and Vuillerme [23] used the joint position error (JPE) test to measure subject's ability to reorient their head on their trunk with eyes closed following full cervical rotation to both left and right sides. Subjects were randomly divided into control and dorsal neck fatigue groups. The investigators observed inconsistent cervical joint repositioning in the neck fatigue group, which they attributed to abnormal afferent input from the cervical joint and muscle receptors.

Revel at al [24] determined that patients with cervical spine pain had less accurate head repositioning performance. To determine cervical kinesthetic awareness, the investigators performed a clinical evaluation of active head positioning in the horizontal and sagittal planes. Thirty adult patients with chronic cervical pain participated in the study. A laser light beam was fixed on top of a helmet and pointed at a target 90cm in front of the patient. Patients wore goggles to block their peripheral vision and the target was movable to accommodate sagittal and horizontal head movement plane. Ten trials of maximal extension and flexion of the head were applied. Their results showed that patients with cervical pain had significantly less accurate head repositioning performance.

Heikkila and Astrom [10] reported that patients with chronic somatosensory dysfunction after whiplash trauma had significantly less accurate repositioning ability of their heads in space with their eyes closed compared to healthy subjects. A total of 40 whiplash injury patients and 34 healthy subjects participated in the study. Whiplash injury patients showed less precision in sagittal plane repositioning head movements. The investigators suggested that this was due to the mechanisms involved in hyperextension and hyperflexion traumas. Patients also demonstrated an overshooting tendency in both sagittal and horizontal plane movements. The investigators suggested overshooting was the result of a mismatch between current proprioceptive information and proprioceptive information coming from stretched antagonist muscles.

Vuillerme et al [34] investigated the effects of cervical muscular fatigue on postural control under multiple sensory conditions. Their results showed that cervical muscle fatigue exacerbated center of foot pressure displacement in the absence of vision. The investigators suggested there is a correlation between neck muscle fatigue and impaired postural stability.

Stapley et al [29] observed increased postural sway in subjects with cervical spine whiplash injuries after fatiguing their dorsal neck muscles. Patients performed isometric dorsal neck exercises for 5 minutes. Postural stability was measured before and after the exercise using a dynamometric force platform. Also, electromyography (EMG) was used to determine the neck muscle fatigue for all subjects. Following the exercise, 7 subjects out of 13 subjects showed signs of fatigue and increased postural sway suggesting a connection between neck muscle fatigue and impaired postural stability. The 6 subjects not reaching fatigue did not demonstrate increased postural sway.

Tjell and Rosenall [31] determined that patients with cervical trauma experienced a change in smooth pursuit eye movement following neck rotation. Their findings revealed the reliance of normal eye movement on authentic sensory input from the spine. Additional evidence supports the role of the vestibular system in eye movement [20]. The vestibulo-ocular reflex (VOR) can be activated by the stimulation of the deep cervical spine mechanoreceptors [13,20].

Padoan et al [20] examined the relationship between neck proprioception and the VOR. Healthy subjects were passively rotated on a rotary chair with their heads passively turned at angle of 70 degrees to either side. The VOR gain tended to be lesser when the subjects rotated their heads turned opposite to the direction of rotation compared to when they were rotated in the same direction but with their head facing forward. Results showed that VOR gain was lower when subject's heads were facing the opposite direction from which the chair was being rotated although their heads had to be facing forward. These results suggest that it is possible to measure the interaction between neck proprioception and VOR in subjects with normal vestibular function. Furthermore, it was determined that atypical stimuli arising from abnormal neck muscle may result in abnormal functioning of the VOR leading to problems in posture and visual unsteadiness.

Given the lack of empirical evidence, the interaction between cervical spine proprioception and the VOR and its impact on humans is not well understood [11,13,20]. We hypothesized that healthy subjects exposed to continual visual flow associated with dorsal neck muscle fatigue during immersion virtual reality would have less postural stability than subjects exposed to continual visual flow without neck muscle fatigue during immersion virtual reality. The purpose of this study was to investigate the effect of

neck muscle fatigue on postural stability during immersion virtual reality.

Methods

Participants

A total of 41 male subjects ages 20 to 39 years old were recruited for this study. Twenty-one subjects were randomly assigned to the experimental group and 20 to the control group. Subjects were pre-screened using a self-report health questionnaire. Exclusion criteria included motion sensitivity, current cervical spine pain or history of cervical spine pathology, dizziness or imbalance due to medication or otherwise, and/or migraine disorder. The study was conducted in the Department of Physical Therapy at Loma Linda University with the approval of the Loma Linda University Institutional Review Board.

Sample Size

Forty-one subjects participated in the study. Sample size was calculated with an estimated effect size of 0.25 between the experimental and control groups. The statistical test used were Mixed models ANOVA with one within subject factor (pre-post) and one between subject factor (assessment type). In order to realize a medium effect, the minimum sample size was determined to be 40 subjects with an alpha level of 0.05 and power of 0.80.

Randomization

Randomization of subjects into the experimental or control group was determined

using computer generated random sequencing.

Study Design

The study utilized a pre and post-assessment analysis with postural stability degree as the primary outcome variable. Postural stability degree measurements were obtained using computerized dynamic posturography with immersion virtual reality (CDP-IVR), (Bertec Balance Advantage-Dynamic CDP) [2].

Data Collection and Balance Assessment

Investigators assessed subjects' postural stability during quiet and dynamic stance using the Bertec Balance Advantage-Dynamic CDP. Subjects stood still on a forceplate with their feet placed at equal distance on fixed points and arms in a relaxed position. A total of 6 trials with 3 measurements for each sensory organization test (SOT) conditions (pre and post) were obtained, with each trial lasting 20 seconds (a total of 60 seconds). Pre and post- tests were performed in both the experimental and control groups. During the assessment, subjects looked forward with their eyes fixed on a target 1 meter in front of them (Fig.1). Two consecutive measures of SOT test conditions 1 and 4, (1) normal vision with fixed support and (4) normal vision with sway-referenced support, with a continual visual flow that was independent of the subjects' movements were performed (Fig. 2.3). Using a computer, signals from the subjects' effort to maintain balance was sampled and analyzed at 1000 Hz following and sway path was computed. The SOT utilizes a Sway Area calculation sway path with equilibrium scores quantified by how well the subjects sway remains within the expected angular limits of stability during each

SOT condition. The following formula was used to calculate the equilibrium score:

$$\text{Equilibrium Score ES} = ([12.5\text{deg} - (\text{the taMAX} - \text{the taMIN})] / 12.5\text{deg}) * 100$$

Twelve and one half degrees is the normal limit of the AP sway angle range. Subjects exhibiting little sway will achieve equilibrium scores near 100, while subjects

approaching their limits of stability will achieve scores near zero. The Bertec Balance Advantage-Dynamic CDP calculated the Equilibrium Score based on Sway Angle, which does compensate for a person's height.

The following formula was used to calculate the sway angle:

$$\text{Sway Angle} = \arcsin (\text{COGy}/(.55*h))$$

The inverse Sin of the center of gravity was divided by 55% of a person's height. The age of subject was not factored into the calculation.

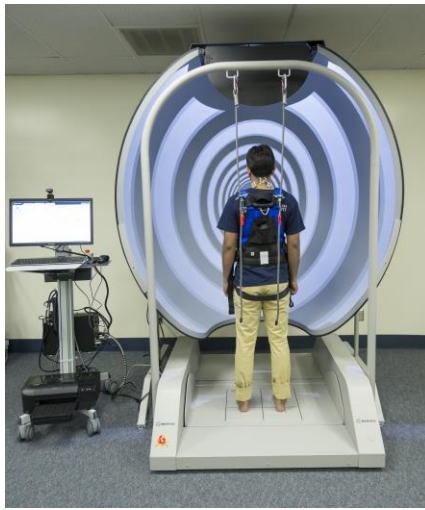


Fig. 1. Subjects stood still on a forceplate with their feet positioned according to a standardized grid and arms by the side. During the assessment, subjects looked forward with open eyes fixed on a target 1 meter in front of them.



Fig. 2. Subjects looked forward with open eyes fixed on a continual visual flow that was independent of the subjects' movements. The optokinetic flow used in the continual visual flow was of thicker lines and with the highest degree per second velocity, determined to challenge the subject's visual perception.

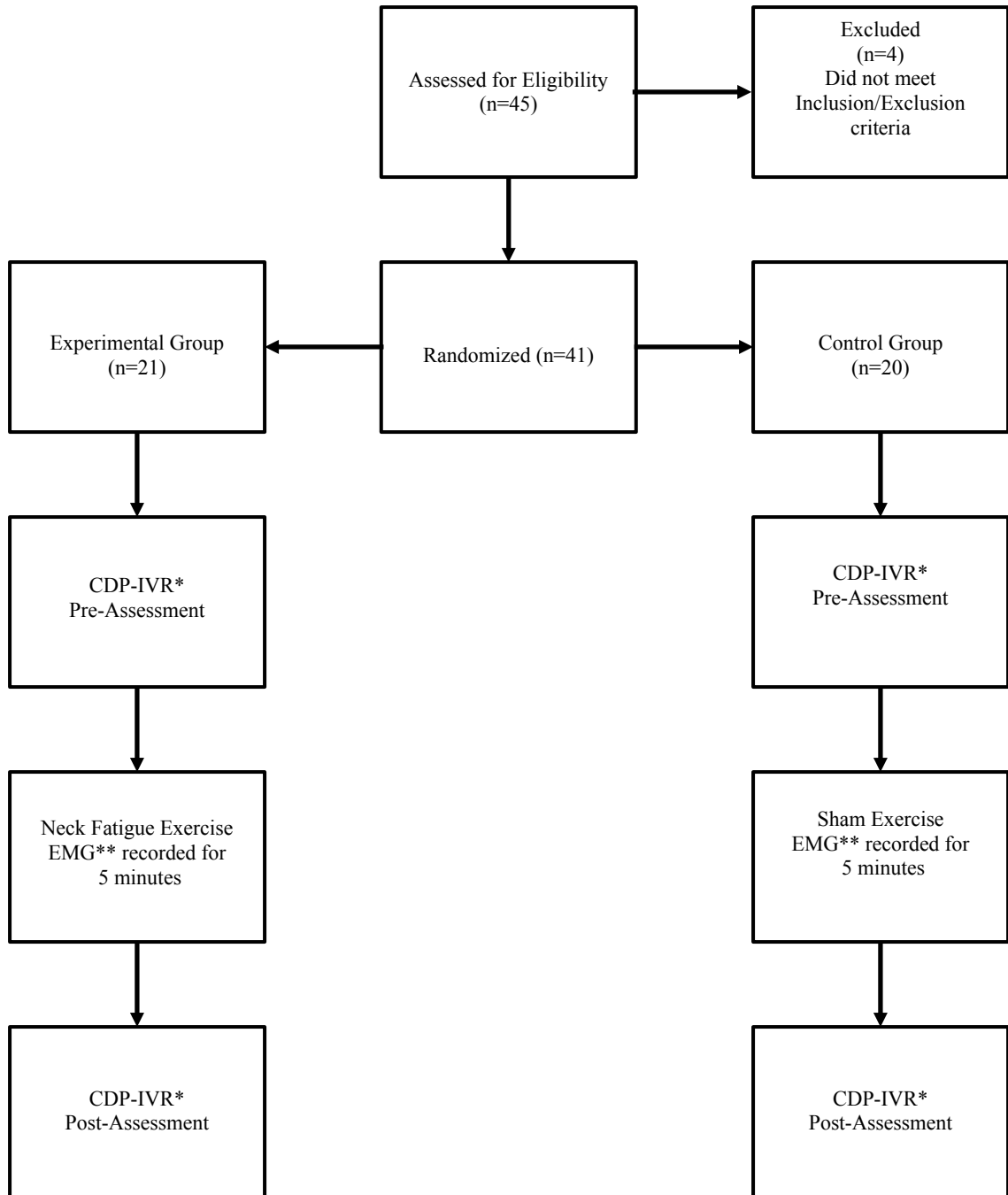


Fig. 3. Consort flowchart diagram.

*Computerized dynamic posturography (CDP) with immersion virtual reality (IVR)

** Electromyography

Neck Fatiguing Protocol and Experimental Procedure

Using bipolar surface electrodes placed 1 cm apart from each other, the investigators recorded the EMG activity of both the right and left dorsal neck muscles (head extensors). The electrodes were aligned longitudinally over the muscle bellies, 2 cm for the body midline and 4 cm below the cranial insertion. The electrodes were left in place for the entire duration of the experiment (Fig.4). EMG signals were pre-amplified (1000 Hz) and filtered at 500 Hz using Noraxon™ MR3 system. Utilizing the Acknowledge software, the investigators computed the EMG amplitude (AMP) of the filtered and integrated signal (area of the envelope) and the signals' median power frequency (MPF) for 10 seconds of 5 fatiguing minute (see protocol below). AMP and MPF were obtained in a similar fashion as in Merletti and Lo Conte (1997); Stapley et al (2006); Yoshitake et al (2001) [19,29,37]. By establishing the changes in AMP and MPF between the first and the last minute of the contracting period, the investigators were able to create a fatigue index using the formula below

Fatigue Index = ratio AMP/ratio MPF

In this case, Fatigue Index = ratio AMP/ratio MPF = (AMP of the first 10 seconds-period of the fifth minute/AMP of the first 10 seconds -period of the first minute) and the ratio MPF = (MPF of the 10 seconds-period of the fifth minute/MPF of the 10 seconds-period of the first minute). Using this index, the investigators classified patients as showing signs of fatigue during the pre-assessment session (fatigue index >1.1 with 1.0 as the null or no change); or no sign of fatigue detected.



Fig. 4. Using bipolar surface electrodes placed on the cervical extensors 1 centimeter apart from each other. The investigators recorded the EMG activity of both the right and left dorsal neck muscles (head extensors). The electrodes were left in place for the entire duration of the experiment for both groups.

The Cervical Spine Isometric Contraction Protocol

A customized neck exercise machine was used and subjects' head and neck were positioned in neutral. Subjects in the experimental group performed a 5-minute neck load of stacked weights equivalent to 35% of their maximum voluntary contraction (MVC) [10,26,29] (Fig.5). During the exercise, EMG AMP and MPF were recorded during the first 10 seconds of each ensuing fatiguing minute. A total of three MVC measurements were obtained (in pounds) using a dynamometer and averaged. To limit involvement of trunk muscles during the MVC and 5-minute isometric exercise, a belt was used to harness the trunk to the exercise machine [26]. Subjects provided verbal feedback of their neck fatigue via a modified visual analog scale (mVAS) of 0 to 10, with 0 being no fatigue and 10 being the most fatigue possible.



Fig. 5. Subjects in experimental group sat with their head and neck in neutral position. To limit the involvement of trunk muscles during the 5-minute isometric exercise, a regular gait belt was used to harness the trunk to the back support.

Sham Exercise Protocol

Four target points were affixed to a wall directly in front of the subject (center, down, left, right) while in an upright sitting position. The sham exercise began with the subject's head in neutral position (eyes facing forward) with instructions to fix their eyes on the center target for 20 seconds. Then subjects were asked to move their head slightly to the right target and fix their eyes on the next target for 20 seconds. Subjects were then instructed to return their head back to the center target for another 20 seconds. This was followed by a one-minute break. The sequence was then repeated for center-left-center and center-down-center. The exercise lasted a total of 5 minutes. The sham exercise was designed to avoid neck muscle fatigue and EMG was used to measure subject's neck muscle fatigue.

Data Analysis

Descriptive statistics were given as mean and standard error of the mean for each continuous variable (SOTs). Assessment of normality was performed using *Kolmogorov-Smirnov* test along with Box and Whisker's plot and histograms. Comparison of means between the experimental and control groups was performed using Independent samples t-test. The mixed models procedure was used in the analysis to test the effect of the different groups (assessment type), time (pre-post) and group x time interaction. Significance was set at an alpha level of 0.05. All data analyses were performed using statistical package SPSS for Windows version 22.0 (SPSS, Inc., Chicago, IL).

Results

EMG Findings

Based on the fatigue index for subjects in the experimental group, 14 of 21 subjects reached the threshold of 1.1 or more. Dorsal neck muscle EMG recordings during the 5 minute fatiguing exercise showed a reduction in the median power MPF and an increase in AMP in 14 subjects (indexes >1.1 were observed in the experimental group) (Fig.6). Subjects in the experimental group sustained an average load of 7.5 kg (Table 1). A significant decrease in MPF was observed during the fifth minute contraction compared to values obtained during the first minute of first fatiguing contraction ($p=0.008$) (Table 2). In total, median frequency readings decreased by 14% during the fifth minute of contraction compared to initial contraction during the first minute. Furthermore, a 40% increase in average AMP was recorded during the fifth minute contraction compared to values observed during the first minute (Table 3). Average results of filtered EMG recordings during the fatiguing periods are reported in Fig.7. Further analysis of variance showed a significant increase in AMP during contraction time ($p<0.001$) (Table 4.). However, subjects in the experimental group who recorded indexes <1.1 did not register significant changes in EMG AMP and MPF between the first and fifth contracting minutes. These subjects maintained an average load of 6.94 kg compared to the other 14 experimental subjects who reached the fatigue index threshold ($p=0.280$) (Table 3). Neck muscle fatigue index was obtained by dividing the median EMG frequency at the end of the contraction period (first 10 seconds of fifth minute) by the MPF at the beginning of the same period (first 10 seconds of first minute).

On average, there was no significant decrease in MPF of EMG following 5

minutes of low-level neck muscle tonic contraction. However, significant decreases were observed for high-level effort (Fig.6). Similarly, the AMP (Fig.7) remained constant from the beginning to the end of low-level effort; however, AMP increased for all 14 subjects for both the first and the second fifth minute contraction periods. AMP was obtained by dividing the AMP at the end of the contraction period (first 10 seconds of fifth minute) by the AMP at the beginning of the same period (first 10 seconds of first minute).

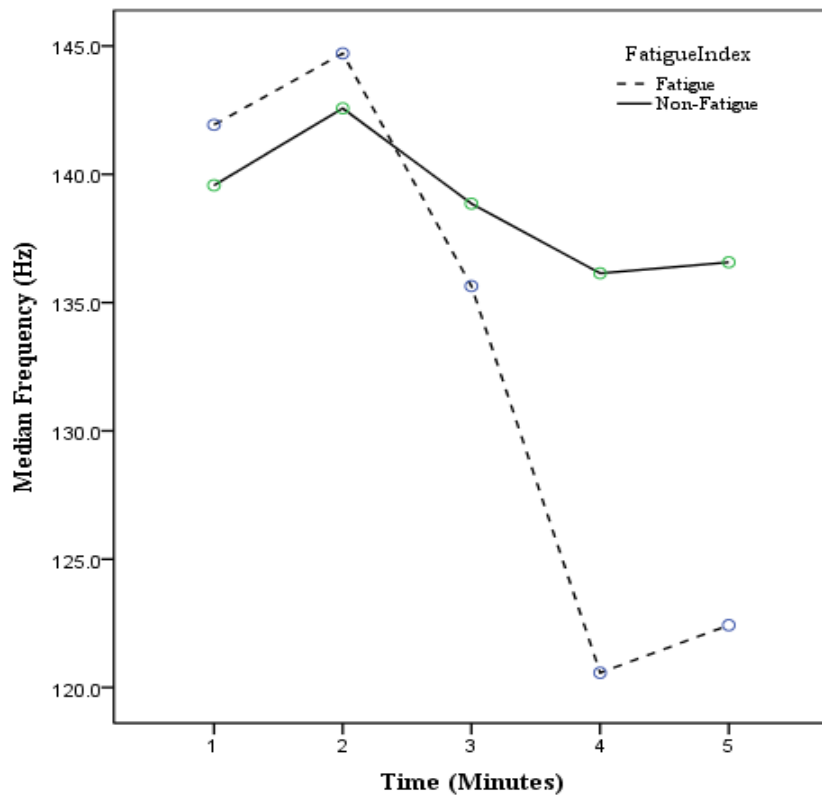


Fig. 6. Experimental subjects reaching fatigue index (N=14) had a reduction in the median power frequency (MPF). Experimental subjects not reaching fatigue index (N=7) showed mild reduction in MPF.

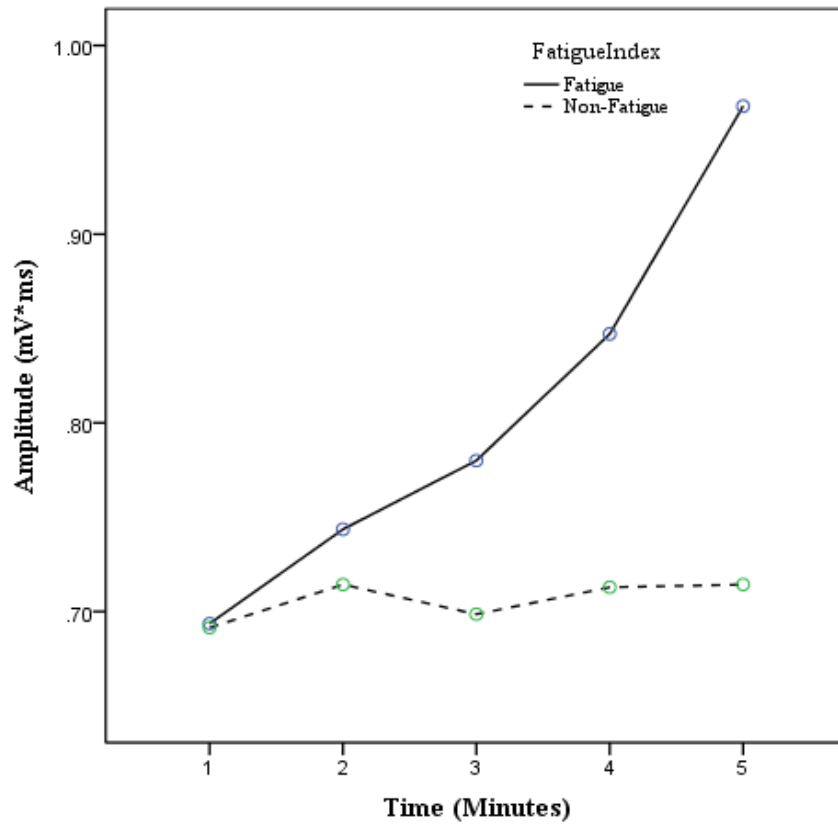


Fig. 7. Experimental subjects reaching fatigue index (N=14) had progressive increase in EMG amplitude (AMP). Experimental subjects not reaching fatigue index (N=7) showed minimal increase in AMP.

Table 1. The mean load weight of experimental group

Experimental Group		Mean	Std. Deviation	P-value
Weight	Fatigue	7.52	2.76	0.280
	Non-Fatigue	6.94	2.36	

Table 2. The mean median frequency of experimental group

Experimental Group	Mean	Std. Error	95% Confidence Interval		Time p-value	Between Group p-value	Interaction p-value	
			Lower Bound	Upper Bound				
MedFreq*	Fatigue	141.93	.787	140.28	143.57	0.008	0.039	0.079
		144.71	1.21	142.18	147.25			
		135.64	1.26	133.01	138.27			
		120.57	5.95	108.12	133.02			
		122.43	1.52	119.25	125.60			
	Non-Fatigue	139.57	1.11	137.24	141.90			
		142.57	1.71	138.98	146.16			
		138.86	1.78	135.14	142.58			
		136.14	8.41	118.53	153.75			
		136.57	2.14	132.08	141.06			

* Median power frequency

Table 3. Experimental group EMG level of change

EMG	Experimental Group	%Change
Amp*	Fatigue	39.67
Amp	Non-Fatigue	3.31
MedFreq**	Fatigue	-13.74
MedFreq	Non-Fatigue	-2.15

* Amplitude

** Median power frequency

Table 4. The mean amplitude of experimental group

Experimental Group		Mean	Std. Error	95% Confidence Interval		Time p-value	Between Group p-value	Interaction p-value
				Lower Bound	Upper Bound			
Amplitude	Fatigue	.694	.005	.682	.705	<0.001	<0.001	<0.001
		.744	.021	.700	.787			
		.780	.012	.755	.805			
		.847	.013	.820	.874			
		.968	.017	.931	1.004			
	Non-Fatigue	.691	.008	.675	.707			
		.714	.030	.652	.776			
		.699	.017	.664	.733			
		.713	.018	.675	.751			
		.714	.025	.663	.766			

Main Findings

There was no difference by group at baseline between age and postural stability degree (Table 5). However, significant differences were observed in post-assessment mean postural stability during SOT1 within ($p=0.019$) and between two groups ($p=0.045$) (Table 6). Additionally, the mean sway in post-assessment during SOT4 within and between two groups interaction was highly significant different ($p<0.001$) (Table 7). It was observed that subjects who were fatigued (experimental) had significantly less postural stability on the moveable surface/platform (SOT4) compared to those who were not fatigued (control) (Fig.8). Nevertheless, there was no difference in maintaining postural stability at stable surface/platform (SOT1) between the experimental and control group (Fig.9). Also, a significant difference was observed in post-assessment postural stability degree at overall SOT between experimental and control groups ($p<0.001$) (Table 8) (Fig.10). On the contrary, the correlation between mVAS and fatigue index in the experimental group was not significant ($p=0.33$) (Table 9).

Table 5. Baseline characteristics of subjects

		N	Mean	Std. Deviation	P-value
Age	Experiment	21	28.86	4.40	0.636
	Control	20	29.45	3.49	
SOT1Pre*	Experiment	21	91.51	3.42	0.182
	Control	20	90.12	3.13	
SOT4Pre**	Experiment	21	51.43	24.38	0.158
	Control	20	41.43	19.66	

* Sensory organization test 1 (normal vision with fixed support)

** Sensory organization test 2 (normal vision with swayed-referenced support)

Table 6. SOT1 within and between groups

		Mean	Std. Error	95% Confidence Interval		Pre-Post p-value	Between Group p-value	Interaction p-value
				Lower Bound	Upper Bound			
Experiment	Pre	91.51	0.72	90.06	92.96	0.019	0.450	0.15
	Post	83.40	2.86	77.62	89.17			
Control	Pre	90.12	0.73	88.63	91.60			
	Post	88.07	2.93	82.15	93.99			

Table 7. SOT4 within and between groups

		Mean	Std. Error	95% Confidence Interval		Pre-Post p-value	Between Group p-value	Interaction p-value
				Lower Bound	Upper Bound			
Experiment	Pre	51.43	4.85	41.63	61.23	0.208	0.728	<0.001
	Post	42.19	5.09	31.90	52.48			
Control	Pre	41.43	4.97	31.39	51.48			
	Post	56.87	5.21	46.32	67.41			

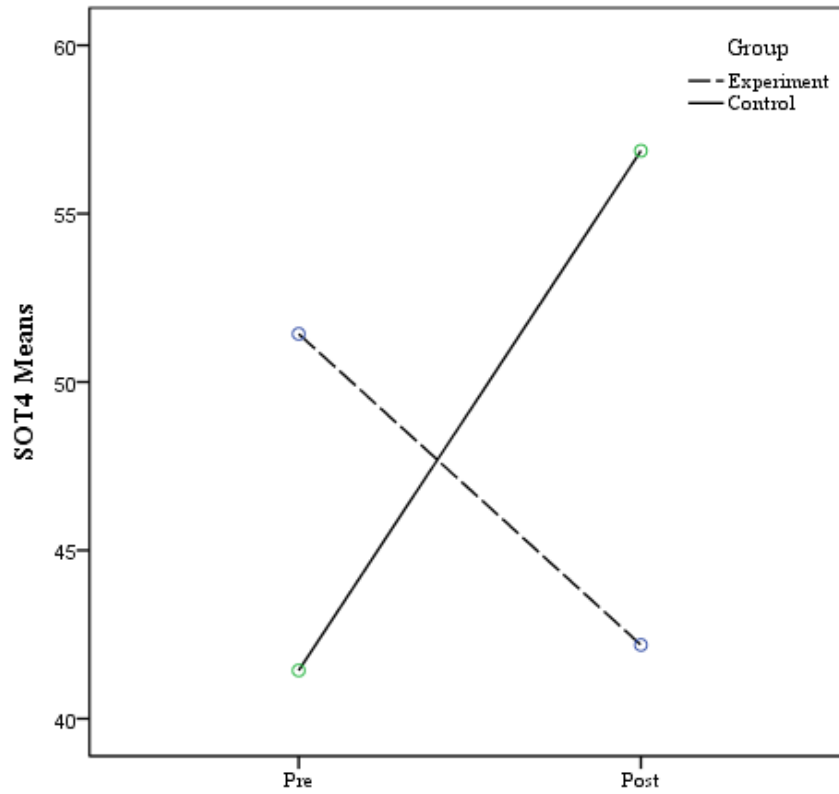


Fig. 8. Post intervention measurements showed experimental subjects reaching fatigue index (N=14) had significantly poorer postural stability in moveable surface/platform (SOT4) compared to control subjects (N=20).

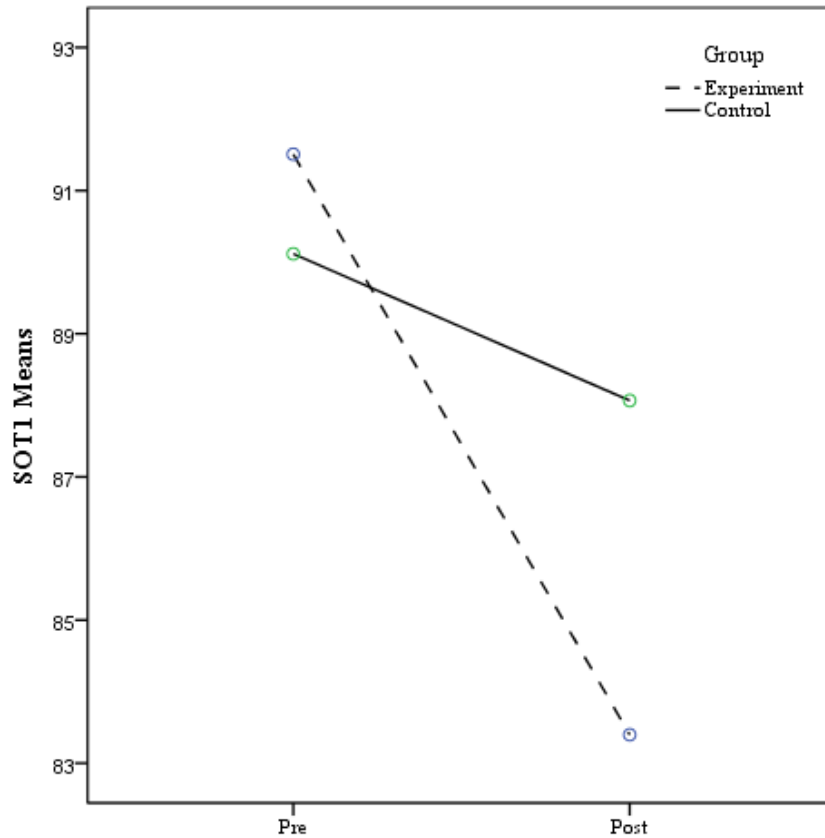


Fig. 9. Post intervention measurements showed experimental subjects reaching fatigue index (N=14) had same level of postural stability in stable surface/ platform (SOT1) compared to control subjects.

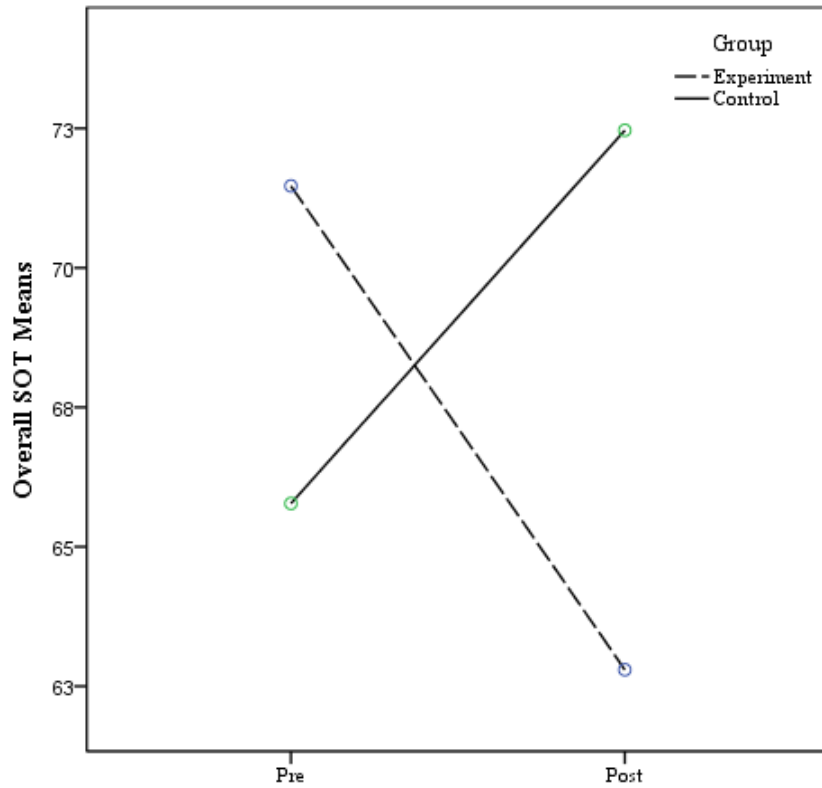


Fig. 10. Post intervention measurements showed experimental subjects reaching fatigue index had significantly poorer postural stability (both SOT1 and SOT4) compared to those who were not fatigued (control).

Discussion

The effect of cervical muscle fatigue on postural stability has been described in numerous studies [8,26,29,34]. Gosselin et al [8] reported that a 25% maximal isometric contraction of the neck extensors for 10 and 15-minute durations produced negative impact on postural stability in young healthy men. Schieppati et al [26] reported that neck muscle fatigue is directly responsible for abnormal postural stability. Vuillerme et al [34] investigated the effects of cervical muscular fatigue on postural control under multiple sensory conditions. Their results showed that cervical muscle fatigue aggravate center of foot pressure displacement in the absence of vision. Also, Stapley et al [29] reported decreased postural stability in subjects with cervical spine whiplash injuries after fatiguing their dorsal neck muscles. All studies results supported that prolonged isometric contraction of cervical extensor would produce significant changes in postural stability. On the other hand, it has been established that vision has a role in subject's postural stability [4,16,17,21,30,33]. Continual visual flow detected by retina (visual background) may lead to either environment-motion or self-motion sense causing postural instability [22,28]. Many researchers have studied the effect of dynamic visual motion on postural stability [3,22]. Peterka and Benolken [22] reported no differences in postural stability AMP between healthy subjects and subjects with vestibular loss. Both groups were subjected to a sinusoidal black and white moving scene. Furthermore, Borger et al [3] examined the influence of dynamic visual environments on postural stability in older adults. Results showed that older adults are more influenced by dynamic visual information for postural stability than young adults. These studies suggest that dynamic visual motion negatively influences postural stability. In the present study, we

investigated the effect of continual visual flow associated with dorsal neck muscle fatigue on postural stability during virtual reality. Subjects in the experimental group experienced a significant decrease in postural stability in post-assessment for both SOT1 and SOT4 conditions. Fourteen of twenty-one subjects in the experimental group reached the fatigue index. Fatigue was induced via five minutes of dorsal neck muscle isometric contraction using 35% of their maximal voluntary contraction [7,10,26]. Fatigue was determined by progressive increase in EMG signal AMP and subsequent decline in signal median frequency during contractions [29]. All subjects in both groups were exposed to continual visual flow that was independent to subjects' movements. Also, subjects' eyes were fixed on the continual visual flow via immersion virtual reality [2]. Investigators suggested that subject's postural stability might have been negatively impacted during the conflict of abnormal visual and neck muscle fatigue afferents. Nevertheless, when comparing pre and post assessment for both conditions, a decrease in postural stability was observed. Although seven subjects in the experimental group did not reach the fatigue index, it is our opinion that at the very least they were partially fatigued. It has been noticed that seven subjects had negative impact in postural stability for post-assessment in both SOT1 and SOT4. Their EMG result showed slight increase in EMG signal AMP with mild decline in signal MPF during contractions. Considering this EMG result, authors suggested that seven subjects in the experimental group might reach the level of being partially fatigued. Also, it is possible that they under-estimated their ability to resist load-inducing fatigue, or they were simply not willing to bear the load [29]. Curiously, the average loads sustained by fourteen subjects were similar to those of seven subjects (7.25 kg) suggesting that the seven subjects not reaching the fatigue index may have been less

susceptible to contraction-induced fatigue [7]. Furthermore, resulting fatigue may not have been exclusively attributed to load on neck muscles, but may also be as a result of individual differences in response to maintained contraction largely attributed to anthropometric measures (the size of the dorsal neck muscles) [29].

Additionally, in the control group when comparing pre and post assessment for both conditions, subjects recorded slight increase in postural stability at SOT1 and also progressive increase in postural stability at SOT4. This observation suggests that training experience may occur for SOT conditions 1 and 4. More postural stability observed at condition 4 may be attributed to complexity and novelty of the task, or the dependence of those tasks on vestibular information [36]. It may be argued that the learning process results from some type of adjustment or adaptation strategies such as increasing ankle stiffness [7,32,36]. Also, reduction of postural stability may occur due to recalibration of sensory information [7,32,36]. However, we suggest that subjects in this study experienced short-term adaptation evidenced by an improvement in equilibrium scores during post-assessment. It's worth mentioning that subjects in this study maintained or advanced their composite scores on the post-assessment suggesting that some form of adaptation ensued during the trial.

When comparing control and experimental groups for both conditions, the results showed that continual visual flow associated with neck muscle fatigue during virtual reality had a negative impact on postural stability of the subjects in the experimental group. Our findings are in alignment with previous studies suggesting poor postural stability resulting from sensory mismatches and possible imbalance of the VOR [11,13,20]. This suggests a disruption in transferred information leading to a possible

disturbance in neuronal connection among the three sensory systems (somatosensory, vestibular, and vision). Previous studies examined this phenomenon; the dorsal neck muscle fatigue attributed to modify the discharge of sensory receptors input, which in turn affected proprioception [26,29,34]. As a result, neck muscle fatigue may affect neuronal connections between the three sensory systems, possibly resulting in the increase in VOR. For this reason, it is important to note that patients complaining of dizziness and/or visual disturbances may be having VOR disturbances of cervical origin due to somatosensory disturbance [20].

Conclusion

Our results demonstrated that dorsal neck muscle fatigue associated with continual visual flow negatively impacted postural stability during immersion virtual reality. Subjects in the control group were able to quickly adapt to the continual visual flow and demonstrated significant improvements in postural stability. In contrast, dorsal neck muscle fatigue interfered with adaptation and postural stability significantly declined. These findings add to the growing body of evidence implicating cervicogenic contributions to postural instability. In particular, the continual visual flow highlighted the influence of the visual system on motion sensitivity and the integrity of the dorsal neck muscles.

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CHAPTER THREE

DISCUSSION

Evidence is building up in favor of effective physical therapy management of CGD. Cervicogenic dizziness may result from a number of factors, ranging from mechanical restriction of the vertebral artery network, cervical sympathetic nervous system irritation, to an impairment of the upper cervical spine proprioceptive input [3,11,13,14,21-24]. Medical history from the patient will often reveal physical trauma to the neck and cervical spine postural faults. To ensure that the exact origin on the patient's dizziness is located, a clinician must perform detailed subjective and physical examinations to rule out competing causes of dizziness. Appropriate interventions will be implemented once CGD has been confirmed.

Cervicogenic dizziness is caused by a number of factors ranging from the mechanical confinement of the vertebral artery network, irritation of the cervical sympathetic nervous system, to the abnormal proprioceptive input from the upper cervical spine [11,13,14,21].

The possibility of mechanical compression of the vertebral artery network may occur when muscles in this region tighten up leading to symptoms associated vertebrobasilar insufficiency (VBI). The vertebrobasilar arterial network starts at the aortic artery through the subclavian arteries, which in turn form into right and left vertebral arteries [2,6,9,12]. The vertebral arteries journey upwards through the transverse foramen of the C6-C1 then horizontally through the posterior arch of the atlas, where they gain entry into the foramen magnum and join to form the basilar artery [6,9]. The anatomical pathway of the subclavian and vertebral arteries is replete with muscles

and bones, which make it likely that a mechanical compromise may occur [6,9]. This would happen if the muscles of the cervical spine tighten as may happen when the neck is rotated. This may in turn lead to a compromise of the vertebrobasilar and collateral arteries resulting in brainstem ischemia and symptoms consistent with VBI. The vertebral arteries journey between the anterior scalene and longus colli muscles as well as under the inferior capitis oblique and intertransversarius muscles. Bone abnormalities and poor spine posture may also add to the compression of vertebral artery and produce symptoms consistent with VBI [6,12,19].

CGD may also be caused by an irritation of the cervical sympathetic nervous system. The cervical sympathetic nervous system travels antero-lateral to the cervical vertebral bodies and side by side with arterial network and cervical musculature [6,12,19]. A compression in the upper cervical spine muscles, bone anomalies, and poor spinal posture may also cause damage to the largest of the cervical spine ganglion, the superior cervical sympathetic ganglion, leading to hyperfusion and CGD of the vertebral and carotid arterial network. This ganglion is located at the level of the second and third cervical vertebrae [13,14,24].

Patients with CGD also present with other symptoms such as ischemia, inflammation, or fatigue of the cervical extensor muscles, which may lead to an abnormal upper cervical spine proprioceptive input. Also, direct neck trauma such as whiplash-associated disorder (WAD) can impair somatosensory information in the cervical spine [28]. The injury that occurs as a result of the trauma can induce fatigue of the spine muscles, which may refashion the discharge-firing rate of sensory receptors, affecting joint position sense of the head and neck as well as postural stability [2,6,9,12,32].

Researchers have postulated that postural stability and head orientation benefits from a sensory mismatch between the multimodal sensory inputs from the upper cervical spine and other systems. These often result in symptoms consistent with CGD [2,6,9,12]. Stapley et al [28] observed increased postural sway in subjects with cervical spine whiplash injuries after fatiguing their dorsal neck muscles. Isometric dorsal exercise was performed on the patients for 5 minute. Postural stability was measured before and after the exercise using a dynamometric force platform. Also, electromyography (EMG) was used to determine the neck muscle fatigue for all subjects. Following the exercise, 7 subjects out of 13 subjects showed signs of fatigue and increased postural sway suggesting a connection between neck muscle fatigue and impaired postural stability. The 6 subjects that did not reach fatigue did not demonstrate increased postural sway.

A bilateral system of cooperation between cervical and vestibular reflexive systems exists. This interaction is known to contribute to head and neck orientation Cervico collic reflex and vestibule-collic reflex, postural control Cervico-spinal reflex (CSR) and Vestibule-spinal reflex (VSR), and oculomotor control Cervico-ocular reflex (COR) and Vestibule-ocular reflex (VOR). The reflexes thrive on a healthy consolidated central nervous system communication, particularly with the vestibular nuclear complex, in order to maintain normal postural balance and visual stability.

Vuillerme et al [25] investigated the effects of cervical muscular fatigue on postural control under multiple sensory conditions. Their results showed that cervical muscle fatigue exacerbated center of foot pressure displacement in the absence of vision. The authors suggested that there is a correlation between neck muscle fatigue and impaired postural stability.

The visual aspect is an important component of the systems. Several studies have examined vision and its role on postural stability [5,34]. Although difficult to isolate, visual input may act synergistically with the vestibular and somatosensory systems. Dynamic visual motion detected by the retina (visual background) may result in either self-motion or environment-motion sense [10,15]. Many studies have examined the effect of dynamic visual motion (rotate or create a tunnel visual scene effect) on postural stability [7,36]. Peterka and Benolken [30] reported no differences in postural stability amplitude between healthy subjects and subjects with vestibular loss, both groups were subjected to a sinusoidal black and white moving scene. The investigators suggested that the somatosensory system in subjects with vestibular loss did not compensate for their vestibular deficit. Also, they suggested that the threshold for the somatosensory cues in healthy subject were greater compared to vestibular cues [30]. Moreover, Borger and colleagues [18] examined the influence of dynamic visual environments on postural stability in older adults. Using a computerized dynamic posturography (CDP) platform, 10 young and 10 older healthy subjects participated in the study. For 3 days a total of six experimental trials were given to each subject. All subjects were exposed to a dynamic sinusoidal black and white moving scene with eyes open for 30 seconds of quiet stance and another 60 seconds of actual scene movement. Results showed that older subjects are more influenced by dynamic visual information for postural stability than young adults

Many studies have examined vision and its role on postural stability. Also, visual input may act synergistically with vestibular and somatosensory systems. On other hand, Postural instability can be caused by many factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma.

Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [3,11,13,14,21-23]. Postural instability can be caused by many factors including aging, neurological disease, vestibular disorders, pharmacology, and cervical spine trauma. Direct cervical spine trauma can lead to cervical spine muscle weakness and alter the discharge-firing rate of upper cervical sensory receptors [3,11,13,14,21-23]. Given the lack of empirical evidence, the interaction between cervical spine proprioception and the VOR and its impact on humans is not well understood [12,25,30]. Our study investigated the effect of neck muscle fatigue on healthy subjects exposed to visual stimuli and compares it with subjects exposed to visual stimuli without neck muscle fatigue. The results demonstrated that dorsal neck muscle fatigue associated with continual visual flow negatively impacted postural stability during immersion virtual reality. Subjects in the control group were able to quickly adapt to the continual visual flow and demonstrated significant improvements in postural stability. In contrast, dorsal neck muscle fatigue interfered with adaptation and postural stability significantly declined. These findings add to the growing body of evidence implicating cervicogenic contributions to postural instability. In particular, the continual visual flow highlighted the influence of the visual system on motion sensitivity and the integrity of the dorsal neck muscles.

Reference.

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APPENDIX A
SELF-REPORT QUESTIONNAIRE



The Effect of Neck Muscle Fatigue on Postural Stability during Immersion Virtual Reality

Health History Screening Form

Date: _____
Subject's ID Code: _____
Subject's Age: _____

Please indicate if you have any of the following:

- | | | |
|--|----|-----|
| • Past or current cervical spinal orthopedic impairments | No | Yes |
| • Past or current vestibular impairments | No | Yes |
| • Past or current neurological pathology | No | Yes |
| • Current medications causing dizziness or imbalance | No | Yes |

APPENDIX B

INFORMED CONSENT

TITLE: **THE EFFECT OF NECK MUSCLE FATIGUE ON
POSTURAL STABILITY DURING IMMERSION
VIRTUAL REALITY**

SPONSOR: **Department of Physical Therapy, Loma Linda
University**

PRINCIPAL

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The Effect of Neck Muscle Fatigue on Postural Stability during Immersion Virtual Reality

1. WHY IS THIS STUDY BEING DONE?

The purpose of the study is to investigate whether neck muscle fatigue impacts motion sensitivity in healthy adults. The results of previous studies suggest that neck muscle fatigue negatively impacts balance and vision during head motions; however, motion sensitivity has not been investigated. You are invited to participate in this research study because you are a healthy adult between 20-40 years of age.

2. HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

40 subjects will be recruited to participate in this study.

3. HOW LONG WILL THE STUDY GO ON?

Your participation in this study will require approximately 60 minutes on a single day.

4. HOW WILL I BE INVOLVED?

Participation in this study involves the following:

If you decide to participate your date of birth, height and weight will be recorded. You will complete a brief health questionnaire concerning current neck pain or history of neck injury. We will then randomly place you into a control or experimental group. Pre and post balance measurements will then be performed as you view a moving visual field. Between pre-post measurements, subjects in the experimental group will perform a neck extension exercise lasting between 3 and 10 minutes. An investigator will provide a visual demonstration prior to your performance. A computerized device will determine when the neck muscles have been sufficiently fatigued during the neck extension exercise. Subjects

in the control group will perform simple eye exercises by looking between targets on a wall in front of them for 5 minutes.

5. WHAT ARE THE REASONABLY FORESEEABLE RISKS OR DISCOMFORTS I MIGHT HAVE?

Participating in this study exposes you to minimal risk because you may lose your balance during the testing procedures. To prevent falling, you will be wearing a safety belt and two researchers will be standing beside you at all times. Also, a mild to moderate discomfort (soreness) may be felt in the upper neck extensor muscles similar to working out at the gym. We will also ensure that the neck exercises are performed correctly and smoothly. There is a minimal risk of breach of confidentiality.

6. WILL THERE BE ANY BENEFIT TO OTHERS OR ME?

You are not likely to personally benefit from participation in the study; however, the expected benefit to science is to determine if neck muscle fatigue affects motion sensitivity. People with chronic neck muscle fatigue due to a variety of disorders including whiplash injuries have been shown to have impaired postural stability but motion sensitivity has not been investigated. Potentially, people with chronic neck muscle fatigue might benefit from specific motion sensitivity training.

7. WHAT ARE MY RIGHTS AS A SUBJECT?

Participation in this study is voluntary. Your decision whether or not to participate or terminate at any time will not affect your present or future relationship with the Loma Linda University Department of Physical Therapy. You do not give up any legal rights by participating in this study.

8. WHAT HAPPENS IF I WANT TO STOP TAKING PART IN THIS STUDY?

You are free to withdraw from this study at any time. If you decide to withdraw from this study you should notify the research team immediately. The research team may also end your participation in this study if you do not follow instructions, miss scheduled visits, or if your safety and welfare are at risk.

9. HOW WILL INFORMATION ABOUT ME BE KEPT CONFIDENTIAL?

Your identity will not be recorded with the research data. We cannot guarantee absolute confidentiality. You will not be identified by name in any publications describing the results of this study. All electronic data will be maintained on an encrypted computer and paper data kept in a locked file cabinet in a locked office.

10. WHAT COSTS ARE INVOLVED?

There is no cost to you for your participation in this study beyond the time involved to participate.

11. WILL I BE PAID TO PARTICIPATE IN THIS STUDY?

You will receive a \$25 gift card after completing the study.

12. WHO DO I CALL IF I AM INJURED AS A RESULT OF BEING IN THIS STUDY?

If you feel taking part in this study has injured you, consult with a physician or call 911 if the situation is a medical emergency. No funds have been set aside nor any plans made to compensate you for time lost for work, disability, pain or other discomforts resulting from your participation in this research.

The Effect of Neck Muscle Fatigue on Postural Stability during
Immersion Virtual Reality

13. WHO DO I CALL IF I HAVE QUESTIONS?

If you wish to contact an impartial third party not associated with this study regarding any question or complaint you may have about the study, you may contact the Office of Patient Relations, Loma Linda University Medical Center, Loma Linda, CA 92354, phone (909) 558-4674, e-mail patientrelations@llu.edu for information and assistance.

14. SUBJECT'S STATEMENT OF CONSENT

I have read the contents of the consent form and have listened to the verbal explanation given by the investigators. My questions concerning this study have been answered to my satisfaction. I hereby give voluntary consent to participate in this study. I have been given a copy of this consent form. Signing this consent document does not waive my rights nor does it release the investigators, institution, or sponsors from their responsibilities. I may call and leave a voice message for Eric Johnson, DSc during routine office hours at this number (909) 558-4632 ext. 47471 or e-mail him at ejohnson@llu.edu, if I have additional questions and concerns.

I understand I will be given a copy of this consent form after signing it.

Signature of Investigator

Printed Name of Investigator

Date

The Effect of Neck Muscle Fatigue on Postural Stability during
Immersion Virtual Reality

15. INVESTIGATOR'S STATEMENT

I have reviewed the contents of this consent form with the person signing above. I have explained potential risks and benefits of the study.

Signature of Investigator

Printed Name of Investigator

Date