Effects of Rhythmic Auditory Stimulation on Distance Walked and Dyspnea in Individuals with COPD

BY

ALISON HERNANDEZ
B.A. University of Miami Florida, 2008
M.S. DePaul University, Chicago Illinois, 2014

THESIS

Submitted as partial fulfillment of the requirements
for the degree of Doctor of Philosophy in Nursing Sciences
in Graduate College of University of Illinois at Chicago, 2018

Chicago, Illinois

Defense Committee:

Eileen Collins, Chair and Advisor
Alana Steffen
Ulf Bronas
Cynthia Fritschi
Lauretta Quinn
David Marquez, Kinesiology

Dedication

तदा द्रष्टुः स्वरूपेऽवस्थानम् ॥३॥

"*tadā draṣṭuḥ svarūpe-'vasthānam*"

For Finding our true self-entails insight into our own nature

I dedicate this thesis and PhD journey, to my parents Susan H. Burdon, and Francisco Hernandez who have always encouraged my academic and life pursuits. They have always allowed me to evolve in my own way, without placing demands or requests. The love, wisdom, and, support they give me is as constant reminder that dedicating yourself to do what you love is most important. They both remind me every day to enjoy the journey and allow this process to reveal my true purpose. My success today and everyday will always be theirs. I would also like to extend this dedication to my grandmother Helga Kmetz who has shown perseverance in life beyond her own lung function.

Acknowledgements

First, I would like to acknowledge and thank my dissertation chair, Dr. Eileen Collins, without which I would have *never* been able to complete my doctoral studies in three years. Her expertise, knowledge, advice and commitment to my progress in this program show her love for research and the future of nursing scholarship. I was extremely fortunate to have her guidance in this program. Every experience I have been lucky enough to have during this program has been thanks to the commitment of Dr. Collins to my doctoral success.

I want to also express my sincerest gratitude to my entire committee, Dr. Steffen, Dr. Bronas, Dr. Fritschi, Dr. Quinn, and Dr. Marquez. Your expertise's and guidance were instrumental during the development of my doctoral thesis. You all have given me the tools upon which I can keep developing as a researcher, and to always aim to do quality work.

I would like to especially thank all the staff at the Veterans Affair Hospital in Hines, Illinois that made my project possible. Thanks to Sue, Jolene, Chris, and Dr. Laghi, without your help I would have not been able to get this far and complete a project I feel so proud of. To the veterans who took their time to participate, you are all heroes who are championing medical advancement and helping us find ways to better serve you.

To the Robert Wood Johnson Future of Nursing Scholarship (RWJ FNS) and staff, I thank you for your generous support financially, and the excellent leadership and mentorship provided thought the program. The RWJ FNS program is a true call to action for all nurses wishing to change the course health care worldwide. I will always be committed to this cause and carry the RWJ FNS name high and proud wherever I may go.

Thank you to the faculty and staff at the College of Nursing who always greeted me with a smile and provided help when needed. A special thanks goes out my friends I made during this journey: Katherine, Luna, Fatimah, Laren (to name a few), your commitment and passion for research continues to inspire me every day. I know the future is bright having your brilliant minds and hearts at the forefront of nursing research.

To my DePaul Bridges family Dr. Aquino and Dr. Lee. You presented me with the opportunity to start my journey towards a doctoral degree in nursing. I thank you for putting your trust in me and motivating me to do so.

I would also like to thank my Illinois Masonic- Advocate Hospital 8 stone manager Cathy Rodriguez and fellow RN's who were always understanding of my limited time to work and encouraged me every step of the way. You always showed enthusiasm and interest in my studies. I look forward to continuing to develop my clinical skills next to all of you.

Last, and certainly not least I want to thank my fiancée Brian Myers (my editor in chief), who has supported me through my entire doctoral program. Your love, encouragement, and dedication always inspire me to try harder. I hope I continue to make you proud.

The essence of all doctorate studies is the love of knowledge. A doctorate of philosophy in nursing is the highest commitment to the attainment of knowledge pertaining to the intimate study of people's health. I am grateful to be in this privileged academic position and look forward to a life of learning.

Table of Contents

List of Tables

List of Figures

Figure Page

List of Abbreviations

6-MWT	6-Miunute Walk Time
6-MWD	6- Minute Walk Distance
BMI	Body Mass Index
DUA	Data Use Agreement
COPD	Chronic Obstructive Pulmonary Disease
CRQ	Chronic Respiratory Questionnaire
FVC	Forced Vital Capacity
FEV_1	Force Expiratory Volume
GDS	Geriatric Depression Scale
HrQoL	Health Related Quality of Life
IRB	Internal Review Board
MBS	Modified Borg Scale
mMRC	modified Medical Research Council
RAS	Rhythmic Auditory Stimulation
SD	Standard Deviation
SF-36	Short Form 36
ST	Sedentary Time
STAI	State-Trait Anxiety Inventory
VA	Veterans Affairs

Summary

The purpose of this study was to compare 6-minute walk distances (6-MWD) and perceived dyspnea in patients with Chronic Obstructive Pulmonary Disease (COPD) under three different walking conditions: walking while listening to Rhythmic Auditory Stimulation (RAS) enhanced music, walking while listening to music as recorded by the artist and, walking with no music. RAS is the process of linking music or metronome accentuated cues with movement to elicit a neurological response to retrain the brain and affect behavior. We hypothesized that individuals with COPD would walk further during the 6-minute walk test (6-MWT) while listening to RAS enhanced music as compared to the 6-MWT distance with no music or distance walked while listening to music as recorded by the artist. An additional aim of this study was to use accelerometer-derived data in the same cohort of individuals to explore amount of time spent sedentary, as well, as factors that may contribute to sedentary behavior.

This dissertation includes the findings of this study in the form of two manuscripts. The first one includes the process and findings from comparing the three 6-MWT, and, the other subjective measures such as health-related quality of life (HrQoL), depression, anxiety, and disease severity. The second manuscript includes the results from the same cohort of participants who wore a triaxial accelerometer during free –living conditions for 7 days. The accelerometer-derived data was used to characterize sedentary behavior and explore its potential correlates.

Effects of Rhythmic Auditory Stimulation on Distance Walked and Dyspnea in Individuals with COPD

Introduction

According to the Centers for Disease Control and Prevention reports, more than 14.5 million Americans are living with Chronic Obstructive Pulmonary Disease (COPD).[1] Exertional dyspnea is the hallmark symptom of COPD and is considered the driver of changes in physical activity and activities of daily living.[2,3] Decreases in physical activity over time leads to physical deconditioning and is an important predictor of hospitalization and mortality. [4] The physical deconditioning that accompanies the disease progression is thought to give rise to many other comorbidities associated with COPD.[3] Perceived dyspnea can be reduced through pulmonary rehabilitation programs. [5] Unfortunately, in most patients, dyspnea reduction and other benefits from pulmonary rehabilitation decrease 6 to 12 months after traditional rehabilitation programs have ended[6-8] and nearly disappear at 2 years.[9] The inability to maintain the benefits of traditional rehabilitation over time exposes patients to an increased risk of physical decline, aggravation of symptoms, hospitalizations, worse health- related quality of life (HrQoL) and even death.[10,11]

The effects of self-selected music have been shown to be most effective in arousing, and decreasing perception of exertion with repetitive endurance type activities.[12] Music has been used as a distractive tool that overrides the neurological attention channels that are usually involved in the conscious perception of unpleasant stimuli such as dyspnea.[5,13-15] Overriding these channels can reduce the conscious perception of dyspnea, motivating patients to walk further.[5] Rhythm processing happens at various levels of the central nervous system. The prefrontal and primary auditory cortex are thought to mediate rhythmic motor entrainment which happens below the level of consciousness.[16] The structural elements of music provide anticipatory rhythmic templates for the brain that supply critical coordinates for optimal motor planning i.e. for walking.[16] Therefore, it is hypothesized that increasing the bass and tempo of music should result in an almost unconscious increase in walking distance.[16] The discovery of the ability of the brain to use rhythmic information to anticipate and plan the execution of movement is called Rhythmic Auditory Stimulation (RAS). RAS is the process of linking music or metronome accentuated cues with movement to elicit a neurological response to retrain the brain and affect behavior.[16] Exposure to rhythmic cues over time provide the brain with optimal motor planning to be able to fixate to physical rhythmic movement patterns. Rhythm and tempo enhancement take advantage of the motivational, affective, and distractive properties of music.[5,13,14] Taking advantage of the motivational and distractive properties of music can also help reduce symptoms of pain, anxiety and dyspnea.[13,14,17] The affective response to music is similar to that observed during behavioral therapy desensitizing individual fears to unpleasant stimulus such as dyspnea in COPD.[18,19] Over time, the use of music can help decrease a patient's conscious perception of dyspnea helping them become less averse to the symptom.[18]

The purpose of this study was to compare 6-minute walk distance (6-MWD) and perceived dyspnea in patients with COPD under three different walking conditions: 1) walking while listening to RAS-enhanced music, 2) walking while listening to music as recorded by the artist and 3) walking with no music. Additionally, HrQoL, anxiety, depression, self-efficacy, disease severity and general health status were explored as potential predictors of performance. We hypothesized that individuals with COPD would walk further during the 6-minute walk test (6-MWT) while listening to RAS enhanced music as compared to the 6-MWT distance with no music or distance walked while listening to music as recorded by the artist.

Methods

Study Sample and Design. Patients with moderate-to-severe COPD were recruited from Edward Hines Jr., VA hospital. Participants completed three 6-MWTs under distinct walking conditions (1- RAS music, 2-music as recorded by the artist, 3- no music). The order of walking conditions was randomized using a table of random numbers to minimize any bias of walk order. There was a 30-minute rest period between each walk. A demographic questionnaire was used to obtain descriptive information about the sample. Pulmonary function test data were used to describe lung function severity. The Mini Mental State Exam (MMSE)[20] was administered to screen for cognitive impairment as beat perception can be compromised in those with cognitive decline. Participants with a score of ≤23 were not be eligible to participate in the study. Exclusions were not made based on use of supplemental oxygen. Participants were invited to participate using a letter of invitation or by responding to a posted flyer. No participant was excluded based on gender or ethnicity. Inclusion criteria were: >40 years of age, $FEV_1/FVC < 70\%$, $FEV_1 \leq 70\%$. Exclusion criteria were: inability to hear, respiratory infection/exacerbations within the previous four weeks, congestive heart failure (New York Heart Association Class III or IV), exercise-limiting peripheral arterial disease (stops exercise due to intermittent claudication), stops exercise due to arthritic pain in the knee or hips (self-report), MMSE ≤23, or assistive devices such as walkers, canes, and being wheelchair bound. It was estimated that a sample size of 30 was needed to achieve 80% power to detect differences (effect size =.83) between walk conditions using a two sided- significance level of α= .05.

Procedure. IRB approval was obtained from the Edward Hines Jr., VA Hospital for the parent study and the University of Illinois at Chicago (UIC). After eligibility criteria were reviewed, written informed consent was obtained. Demographic information, a medical history, height and weight were obtained. Body height and weight were measured using standard anthropometric procedures using a standardized scale and stadiometer. The patient's preferred walking cadence was calculated in order to match the tempo of the music as recorded by the artist to the patient's individual preferred walking cadence; the tempo of the RAS walk was set about 5-10 beats per minute higher than the baseline cadence.[21] Participants rested for 15 minutes before performing the first 6-MWT. During this time, participants were provided a list of songs of popular songs/genres to choose from for walks involving music (genres include: pop, country western, big band, gospel, classic rock, jazz, and blues). Familiarity with music is important as it increases arousal and physical response to music.[18,21,22] All songs available for selection were arranged in 6-minute loops to fit the 6-MWT time. The songs were preloaded onto iPod® Touch and Bose® stereo earphones were placed on participants during walks involving music. Two separate playlists with the same songs were created for the iPod® Touch. One list contained the songs for selection in their original form (as recorded by artist) in 6-minute loops, and the second playlist contained the same songs with RAS modification (at 5-10 beats above their usual tempo ranging from 90-150 beats per minute) also in 6 minute loops. RAS tempo modifications were made using Audacity® software (version 2.1.2!). Participants were not alerted to differences in music for both walks involving music. Participants held the iPod® while walking**.**

Standard testing procedures for the 6-MWT for individuals with COPD were implemented as determined by the American Thoracic Society (ATS) guidelines.[23] The major exceptions to the ATS Guidelines were that patients were not coached and they were not notified of how far along they were in the walk. Participants were asked to walk up and down a 100-foot-long corridor as fast as they could without running. They turned around a cone placed in the corridor at each end of the walk. Participants were allowed to stop and rest if needed. Participants were instructed to advise the investigator when they began to feel short of breath or breathless. Using the 6-MWT we determined maximal walking distance, cadence and perceived dyspnea free time in meters. Vital signs (blood pressure, heart rate, and SpO_2) and perceived dyspnea using the modified Borg scale were obtained prior to and after every 6-MWT to ensure patients safe return to baseline. Two study coordinators were used to administer 6-MWT. The study coordinator administering questionnaires set up and started the song selected on the iPod for the walks involving music (RAS-enhanced and music as recorded by artist) and counted the participant's steps at 1, 3 and 5 minutes to assess cadence during the walks. The second study coordinator, who was blinded to the music conditions, kept track of time, number of laps, distance walked, dyspnea rating, and rating of perceived exertion. Participants were asked to rate perceived dyspnea before initiating the walks, at onset of dyspnea and at the termination (peak) of walks using the modified Borg Scale. Participants rested for 30-minutes between walks and continued to complete study questionnaires during this time.

Measures

Walking Cadence. Participants were asked to walk at a normal speed on a flat surface for 60 seconds to determine their preferred walking speed using steps/minute.[24] The researcher followed behind and counted the number of steps. The number of steps/minute was recorded and used to calculate the tempo of the music for the music walks. Additionally, walking cadence was measured three times during the 6-MWT. One researcher counted the number of steps that the participant took during the 6-MWT between 1 and 2 minutes, 3 and 4 minutes, and 5 and 6 minutes.

6-MWT. The 6-MWT is a reliable and valid measure used to determine the distance subjects can walk in six minutes.[25] It is a submaximal test of functional capacity.[25] Although it does not provide specific information about each biological system, it provides a global assessment of all systems involved in exercise and correlates with quality of life measures.[26,27] Average distance walked for individuals with COPD has been reported as 238-388 meters and walking < 200 meters is considered predictive of hospitalization and mortality.[28] Construct validity is supported by moderate correlations between the 6-MWT and the cardiopulmonary exercise test ($r= .44$, $p = .0013$).[29] Additionally, the 6-MWT is moderately to strongly correlated with peak work capacity ($r= .59$ to $.93$, $p= .05$) and physical activity ($r=.40$ to $.85$, $p= .05$) further supporting validity. The 6-MWT is a reliable measure with intra-class correlations from .82 to .99.[27] As noted above, ATS guidelines[23] were followed with the exception of letting the participant know how far along they were in the walk. Interrupting patients during the music walks would disrupt the rhythm created with the music and draw attention to their breathing making it difficult to ascertain if music provided a distraction from dyspnea.

Self-Efficacy for Walking. The Self-Efficacy for Walking questionnaire consists of 10 questions asking individuals to rate how confident they are that they can successfully walk different distances at a moderately fast pace without stopping (to increase heart rate and work up a sweat). The answers are measured on a scale from 0% (not at all confident) to 100% (highly confident). Validity is supported by high correlations between the self-efficacy scale and the physiological measures such as vital capacity, walking, general exertion, climbing, and lifting.[30]A moderate relationship between walking efficacy and FEV_1 further supports validity of the instrument ($r=.44$, $p<.05$).[30]

Self-Efficacy for Managing Dyspnea. This questionnaire[31] was used to measure the participant’s confidence in keeping shortness of breath from interfering with walking or from doing what they want to do. This questionnaire is composed of one statement, “How confident are you that you can keep your shortness of breath from interfering with what you want to do?” measured on a 1-10 scale (higher scores indicating more confidence). Correlations for the measure range between -.35 to .29 (p= <.001).[31]

Modified Borg Scale (MBS). The modified-Borg scale was used to measure dyspnea and overall fatigue before, after, and during the six-minute walks.[2,32,33] This is an interval, self-rated scale in which symptoms of breathlessness and fatigue were rated between 0 (not at all) and 10 (maximal). Participants had an option to choose .5 for “very, very slight (just noticeable). The MBS was designed as a quick, self-assessment to reflect a person’s severity of dyspnea/ fatigue in general and during any treatment modalities. This tool is especially useful tool in the laboratory producing good inter-rater reliability.[34] The MBS scale is considered a reliable measure of dyspnea.[27,32] Validity is supported by significant correlations between the MBS scores and changes in peak expiratory flow rates (PEFR) from pretreatment to post treatment (r= -.42, P<0.001).[24, 35] Construct validity is supported with a reasonable degree of convergence between the MBS and measures of dyspnea (r= .48, p=.01).[36] Lastly, statistically significant correlations have been found between the MBS scores and peak exploratory flow rate in patients with COPD[35,37] further supporting validity.

The scale was printed on paper with a 20-point type font size to easy readability during the walk.[25] The participants rated their dyspnea before the start of the walks so that they could become familiar with the rating scale. Onset of dyspnea was defined as the initial time when the participant reported any dyspnea.

Modified Medical Research Council Scale (mMRC). According to the Global Initiative for Chronic Obstructive Lung Disease 2017 report,[38] the mMRC is a standard measure for assessing breathlessness. The mMRC is an easy to use, situational measure to quantify secondary responses to dyspnea and requires recall.[39] The patient selects a grade on 5-point scale that describes everyday situations or activity levels provoking breathlessness and impairment and produces a single score (0, indicating "I only get breathless with strenuous exercise to 5, "too breathless to leave the house or breathless after undressing").[34,40] Individuals are assigned to one of five grades. A one-unit change indicates a change in disability; a lower number indicates the less disability. The mMRC has been used to categorize patients in pulmonary rehabilitation. [33,34,39,41] Test- retest of the mMRC has been reported as r=.82 (p < .001).[42]

Chronic Respiratory Disease Questionnaire (CRQ). The CRQ is a 20-item, disease-specific quality of life questionnaire that also assesses secondary responses/impact of dyspnea.[39] The questionnaire takes about 15 minutes to administer via interview. It was designed to determine how the lives of patients with chronic airflow limitation are affected by the illness and the perceived impact of symptoms and limitations on quality of life.[43] The 20 questions on the CRQ measure four dimensions: dyspnea, fatigue, emotional function, and the patient's feeling of control over the disease (mastery). The dyspnea subscale on the CRQ asks individuals to identify activities of importance to them, scored 1 = most dyspnea to 7= least. The CRQ has good test-retest reliability (r= .73) and is moderately correlated with other measures like the SF-36 (r= .66) supporting validity.[44-46] An average change of 0.5 per item within the subscale is considered clinically significant change.[43,47] Waterhouse, Harper, Marsh, Jones, Brazier, Howard [48] reported internal consistency for the domains of the CRQ as follows α=.64 (dyspnea), α= .80 (fatigue), α=.86 (emotional function), α=.84 (mastery). Lacasse, Wong, Guyatt [46] reported that the CRQ provides an approach to quantify the impact of dyspnea, as opposed to the initial response or intensity of dyspnea and distinguish between those patients with more quality of life impairments.[39,46] Cronbach alphas for the CRQ dyspnea, emotion, fatigue, and mastery scales for this study were (α =.895, .880, .832, and .875) respectively.

Pulmonary Function Tests (PFT). PFTs are used to measure the lung ventilatory and diffusion capacities. This information can be attained by measuring flow rate during maximal expiration. The patient is asked to inhale maximally and then exhale as hard as they can. Volume exhaled in the first second is called forced expiratory volume, or FEV_1, and the total volume exhaled is the forces vital capacity or FVC. [49] Normal values range from 80-120% and are based on age gender, height. In obstructive disease, such as COPD, the FEV_1 is reduced much more than FVC. [49] Pulmonary function values were obtained from the patient's medical record. Pulmonary function tests were accepted if they were conducted within the past 2 years and there were no major changes in the patient's medical condition. Two years was chosen as acceptable since lung function decline in patients with COPD occurs slowly over time at approximately 25±23 mL/yr.[50] Patients severity of lung function were then characterized according to GOLD stage[51] (*Table 1*).

Short Form-36 Health Survey (SF-36). The SF-36 is composed of 36 questions designed to assess general Health-related Quality of Life (HQoL) and quantify perceived physical function and mental health.[10,52,53] It is a patient reported survey that takes approximately 10-15 minutes to complete. The SF-36 consists of eight subscales (vitality, physical function, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health), which are weighted; the scale is then transformed to a 0-100 scale. A higher score is better. A study by Parshall, Mapel, Rice, Williams, O'Reilly [54] found that the SF-36 domains were significant and stable predictors of HrQoL in COPD patients over time.[55,56] This measure was used to help describe the sample. The SF-36 scale has high correlations (r=0.96) with other general health ratings supporting its validity. [53] Internal consistency of the SF-36 has been reported as Cronbach's α>.85 supporting reliability.[53,57]

Charlson Comorbidity Index. The Charlson Comorbidity Index is used to predict mortality for patients who have a range of comorbid conditions. Each condition is assigned a score depending on the weighted risk of death associated with it (1 = the lowest risk to 6 = the highest). The total score is computed at the end of questionnaire, with higher scores indicating a higher health risks. It was originally designed to classify comorbidities and stratify patients in order to control for the confounding influence of comorbid conditions.[58] This is a validated measure and widely utilized index.[59,60] Comparison with other co-morbidity indices show correlations to support concurrent validity ($r \geq .40$).[61]

Anxiety. Anxiety was measured using the State-Trait Anxiety Inventory (STAI). The STAI is a self-report measure of both state (20 items describing statements about how they feel right now) and trait anxiety (20 statements asking participants how they feel generally). In these 40 statements, participants respond using a 4-point rating scale ranging from 1 (not at all) to 4 (very much so) in terms of explaining how they feel.[62-64] The STAI is a valid and reliable measure for anxiety with high internal consistency α=.96 for men and α= .89 for women.[65] Item-total correlations ranged from r=.49 to .64 for the state scale, and .38 to .69 for the trait scale.[66] Other findings included support for reliability, with one-week test-retest correlations ranging from r = .78 to .83 for the trait scores, compared to r=.69 to .76 for state scores.[67] The Cronbach's alpha's in this study were state (α= .71), trait (α =.697).

Depression. Depression was measured using the 15-item Geriatric Depression Scale Short Form (GDS-SF).[68,69] The GDS-SF was created as a brief and easy way to screen healthy and ill older adults for depression. The scale is administered and scored quickly (~ 7 minutes). The response format of the 15-item GDS-SF is a dichotomous answer, yes/no, indicating how patients felt in the last week. The 15-items included in the GDS-SF are those that have the highest correlation to depressive symptoms from the initial GDS validation studies. A result of 5 points or more indicates *possible* depression, while a score of 10 or more is indicative of depression.[70] Any score higher than five requires further evaluation for depression. The tool has been widely validated in the older adult population and has a high sensitivity of 80% and specificity of 100% at a cutoff score of 11.[71] The validity of the original GDS was tested by comparing it with the Hamilton Rating Scale of Depression (HRS-D) and the Zung Self-Rating Depression Scale (SDS); it has been tested extensively in a range of older adult ages and is a valid and reliable tool for depression screening.[71-73] Internal consistency reliability is supported with a Cronbach's (α = .94).[71] Cronbach's alpha for the GDS in our study was (α=.669). No participants screened positive for depression.

Mini Mental State Examination (MMSE). The MMSE was used to screen for cognitive impairment prior to study enrollment. Walking to rhythmic cues such as RAS requires attention and higher information processing capabilities which is compromised in individuals with cognitive impairment. [74] The MMSE takes 3 minutes to administer and is an accepted tool to detect cognitive impairment.[20,75,76] Participants are asked to draw a clock and recall words given at the start of the test. These components allow for quick assessment of many cognitive domains including cognitive function, memory, language comprehension, visual motor skills, and executive function. Successful completion ensures that that patients are able to understand instructions. Tombaugh[77] reported the internal consistency of the MMSE as =.96 and a test-retest reliability is *r*=.80. Sensitivity is reported at 87% for the cut off scores of 23/24.[78]

Construct validity is supported with positive correlations with other cognitive measures ranging from r= -.66 to -.93. [79]

Statistical Analysis

Descriptive statistics (mean, standard deviation) were used to describe the sample and results. Paired-samples t-tests were used to compare the walking distances between pairs of the three walking conditions (no music to music, music to RAS, no music to RAS), onset of dyspnea and peak dyspnea. Analysis of variance (ANOVA) was used to test if there were differences in walking distance based on walk order. Pearson r correlations were computed to assess if changes in onset of perceived dyspnea were related to a change in walking distance or walking cadence and to determine if there was a relationship between six-minute distance walked and age, co-morbidities, disease severity, quality of life, depression and anxiety.

Results

Sample. Twenty-five, older adult men, (age = 70.7 ± 4.5 years) with moderate-to-severe COPD (FEV_1 = 47.4 ± 9.7% predicted), were recruited and completed the study protocol. Six participants reported used supplemental oxygen (either to sleep, exercise or as needed at home). Only three used supplemental oxygen to complete the study protocol. See *Table 2* for additional demographic information. There were no adverse events related to the study procedure.

Patients had a mean baseline cadence of 103 (±8) steps/minute. Patients walked 12 m further in 6-MWT when listening to RAS enhanced music (463 ± 72 m) when compared to walking without music (451 ± 81 m); t (24) =-2.63, p=.015) or walking with music as recorded by the artist (451 ± 80 m); t (24) =-2.26, p=.033) (see *Table 3*). There were no differences in distance walked between the no music condition and the music as recorded by the artist condition (t (24) =-.50, p=.960). There were no differences in the onset of dyspnea or the perception of dyspnea at peak exercise (i.e. dyspnea at the end of each respective walk) amongst the different walking conditions (*Table 3*).

Walking cadence measured between minutes 1-2, 3-4, and 5-6 for all three walking conditions are reported in *Table 4*. Walking cadence was significantly greater at the 1-2 (p=.005), 3-4 (p=.002) and 5-6 (p= .004) minute measurement point when comparing RAS to no music. Walking cadence was also greater at the 5-6-minute time point when the RAS condition was compared to the music condition (p=0.003). Finally, there was also an increase in walk distance between minutes 1-2 in the no music and music as recorded by the artist condition (p=.022).

Moderate to strong relationships were identified between the onset of dyspnea and the distance walked with no music (r=.450, p=.024), music as recorded by the artist, (r=.737, p<.001) and RAS walking conditions (r=.626, p= .001) (*Table 5*)**.** Scores for anxiety, depression, co-morbidities, disease severity, HrQoL, secondary response to dyspnea and how they related to distance walked and dyspnea are reported in *Table 6.* Distance walked for each of the walks was also related to perceived dyspnea in daily life as measured by the CRQ (no music, r=.443, p=.027; music as recorded by the artist, r=.519, p=.008; and RAS, r=.498, p= .011). No relationship was found between levels of anxiety, depressive symptoms, disease severity, HrQoL, comorbidities, pack years smoked and distance walked or onset of perceived dyspnea.

There was no difference in distance walked based on the order in which the walk occurred for any of the walking conditions. A one-way ANOVA assessing differences in walk order for each walking condition follows: no music (F= 0.37, df= 2, p=.964), music (F= 0.277, df= 2, p=.761), and RAS (F= .385, df= 2, p=.685).

Discussion

The overall findings from this study are that 6-MWD was greater during the RAS enhanced walking condition than between the music as recorded by the artist and no music walking conditions. Walk cadence in all three-minute intervals were increased when comparing RAS and no music walking condition. Additionally, no significant difference in onset or peak dyspnea was found when comparing walks.

Finding a greater walking distance under the RAS 6-MWT and no significant difference in distance walked between the no music and music as recorded by the artist walking condition, builds on the evidence that the RAS enhanced music may trigger subconscious neurological pathways that affect motoric response to rhythm and tempo.[16,80] The clinically important difference for an intervention for 6-MWD in patients with COPD ranges from 25-35m.[81,82] The difference in our sample was 12 m; although this value was statistically significant, it is not considered a clinically important difference. It is unknown whether this increase in walking distance from one walk to another, used across regular exercise training sessions would translate into a clinically important difference post-rehabilitation using RAS. Our patients walked less distance (451±81 meters) compared to healthy older adults (571 ±90 meters).[83]

Music makes it easier for patients to stay motivated, and achieve greater gains in distance covered by following the tempo of the music.[5,17,18,21,22,84] Bronas, *et al.* conducted a similar study in patients with peripheral arterial disease and found that patients walked 22 meters and 21 meters further when listening to RAS-enhanced music compared to no music and music as recorded by the artist respectively.[80] Our findings identified lesser gains in 6-MWD with RAS over music as recorded and no music which may be due to the differences in clinical manifestations of dyspnea versus claudication pain. Dyspnea may be perceived as more uncomfortable and potentially life-threatening than claudication pain and thus avoided. We only identified one additional study that investigated the use of RAS enhanced music with patients with COPD.[85] Ho *et al.* used RAS-enhanced music to *prescribe* walking intensity for a supervised and home-based exercise program in Korean patients with COPD.[85] Ho, *et al.* demonstrated that using RAS enhanced music to prescribe walking pace during an exercise intervention helped participants achieve higher maximal 6-MWD upon completion of the study (243 ± 135 m versus 306 ± 107 m, $p < .001$).[85] While our study did not use RAS enhanced music to prescribe exercise intensity, the findings support the idea that RAS enhanced music may increase 6-MWD in patients with COPD.

We reported cadence measures between minutes 1-2, 3-4, and 5-6 for all three walking conditions. A significant increase was noted across all three-minute intervals when comparing the cadence of the RAS condition to that of No Music. Mean walking cadence during a 60-second hall walk prior to testing was 103 steps/minute. Reported mean cadence (steps/min) for older adults is around 100 steps/60 seconds.[86] RAS songs were prescribed at 5 to 10 beats above the individual's preferred baseline cadence, and individuals were able to match and sustain this elevated cadence (110 ± 12 steps/minute). This observation may support the premise that beat perception mechanisms can be neurologically entrained.[16] However, it is important to note that the difference in step count was very narrow amongst all walk cadence conditions in all minute intervals. Furthermore, most interventions reporting the use of music tempo to prescribe walking pace have been used during an intervention requiring the participant to consciously attempt to walk to the beat of the tempo.[85] Physiological auditory- motor coordination requires an increased number of steps in order to adjust gait to beat, and acquainting participants to the beat allows for more time and salience.[22,24] Gait will couple best to a beat closest to the participants preferred cadence, thus increasing walking pace comes at the expense of auditory-motor coordination.[12,87] This may suggest that the 5-10 beat increase for the RAS condition may have been too indiscriminate of a range to have an effect, and, that the sample size, age and disease severity too homogenous and not variable enough. Further investigation is warranted on how to precisely prescribe a cadence rate that promotes safe prolonged bouts of movement without compromising gait patterns in this patient population.

No significant difference in perceived onset of dyspnea or peak dyspnea was found. On average, participants consistently reported slight to moderate dyspnea per the Borg scale. The lack of an increase in dyspnea during the RAS walk, where greater distance was covered, could indicate that patients were less aware of the symptom, as intended. Participants in our study may have been less aware of their dyspnea during the RAS walks and thus, able to walk further without stopping or having to focus on managing the symptom. We cannot rule out that the increase distance walked was not clinically significant so there was no increase or earlier onset of dyspnea. When examining the onset of dyspnea results, it appears that onset of dyspnea occurs later and peak dyspnea is less during the music and RAS walks compared to the no music walk. Previous studies have shown that the use of music as a distracting tool for dyspnea can help enhance physical performance.[5,12,87] It is possible, in our sample, that music made no difference in the onset of dyspnea or peak dyspnea level. This finding could also reflect that participants were not pushing themselves beyond a level of dyspnea they felt comfortable with. Neurologically, music is thought to override the attention centers of the brain where we process noxious stimuli such as dyspnea and help release endorphins while generating feelings of calmness.[88] Chronic feelings of breathlessness can provoke anxiety and real fear.[18] Desensitization and distraction have shown to be effective in reducing dyspnea and anxiety.[18,89-

[91] For this reason, music has been used extensively as a cognitive behavioral distractive strategy to increase physical performance in chronically ill patients diverting them from uncomfortable symptoms. [5,13-15] Conversely, familiarity to music is a critical component for arousal during exercise.[24,87] While participants chose from a list of songs, this list was limited and could have had an impact on the motivational qualities. Bauldoff, *et al*. reported that perceived dyspnea was reduced during the 6-MWT coupled with an increase in walk distance in the group that received the music compared to the group that did not during a home-based walking program.[5] Additionally, patients assigned to the music group reported less dyspnea during activities of daily living (ADL).[5] Other studies by, Tsai, von Leupoldt, Bellini,[13,15,92] have also found evidence to support the use of music as a distractive tool for the management of uncomfortable symptoms. Finding no significant difference in onset or peak dyspnea among the walks further supports the use of music as a distractive strategy in this patient population.

Participants were instructed to report onset of dyspnea during 6-MWT. Twenty-five participants provided a rating for peak dyspnea (once walk concluded). We asked participants to alert staff when dyspnea was first noticeable during 6-MWT (onset of dyspnea), but did not remind participants to do this throughout the walks as to not to alter the distractive effects of the RAS and/or music. Onset of dyspnea was however associated with 6-MWD in all three walks *(Table 6)*. We still cannot rule out that participants forgot the initial instructions to self-report onset of dyspnea, or perhaps, the music conditions did in fact distract them from the onset of the symptoms. An additional explanation for this finding is that the sample was composed entirely of men and there is evidence to suggest that men tend to underreport symptoms of dyspnea compared to women.[93-97] Lastly, a type II error may have occurred in that the sample size may have been too small and variability in dyspnea onset too great to detect a significant difference in dyspnea onset.

Patients walked the furthest under the RAS walking condition and perceived dyspnea levels at the end of the walk did not increase significantly. Our findings of no change in dyspnea in light of walking further may or may not provide preliminary support of the notion that RAS provided distraction from the dyspnea. The other possibility is that walking an additional 12 meters may not have been a clinically significant increase in distance to affect an increase in dyspnea.

There has been mixed data on the significance between function, anxiety, depression and pulmonary function in the COPD patient population.[98-100] In our study, there were no significant relationships between the 6-MWD and variables such as anxiety, depression, and pulmonary function. Pirraglia, *et al.* reported that improvement of depressive symptoms in pulmonary rehabilitation were associated with improvements in HrQoL measures.[100] One could postulate, that addressing depression in pulmonary rehabilitation could lead to greater gains in HrQoL for this patient population; this may then translate into better all-around helath.[100] Our sample was small, and did not meet clinical depression cut off scores per the GDS (1.68 ± 2.08). The distance walked on each of the walks was associated to perceived dyspnea in daily life as measured by the CRQ (no music, $r=.443$, $p=.027$; music as recorded by the artist, $r=.519$, $p=.008$; and RAS, $r=.498$, $p= .011$). Distance walked increased as patients scored higher (better) in the dyspnea CRQ domain. These findings are similar to those reported by others.[100,101]

Strengths and Limitations

The sample was composed entirely of older, male veterans who were mostly white. As such, our results are not generalizable to women or minorities. Patients that participated in this study may have been those inclined towards partaking in exercise rehabilitation, and thus not be as representative as the general population. Our aim was to recruit 30 participants to meet our goal sample size (as determined by our power analysis). We had 5 participants who were recruited and were not able to participate due to medical issues on the scheduled day of study enrollment. This smaller sample size may have resulted in a Type II error.

Randomizing the three walks allowed us to control for learning and order effect on the 6-MWT. Time is a critical component to RAS. In gait retraining practice where RAS has been most studied, patients are initially exposed to the RAS before starting training. This allows the brain more time to interpret rhythm cues and prime itself for movement. We did not prime participants to music to limit study participation burden, and wanted to keep participants blind to walking condition. Although we did see significant increases in walking distance under the RAS condition, future studies could investigate if priming before RAS can even further increase walking distance.

Conclusions

Older adult veterans with moderate-to-severe COPD walked farther under the RAS condition with no significant increases in dyspnea. Whether this difference is clinically meaningful is to be determined. This study gathered further evidence that walking under RAS enhanced music may have an effect on 6-MWD in veteran patients with COPD. Dyspnea was not affected by music, enhanced or not, in our study. Further study is needed on larger, more varied samples of participants to test the effectiveness of RAS-enhanced music on distance walked and dyspnea in patients with COPD.

References

1. National Center for Health Statistics. Health USwSFoRaEHDH, MD: US Dept. Health and Human Services; 2016. (http://www.cdc.gov/nchs/hus/) Accessed June 2016.

2. Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med.* 2006;173(12):1390-1413.

3. Scano G, Innocenti-Bruni G, Stendardi L. Do obstructive and restrictive lung diseases share common underlying mechanisms of breathlessness? *Respir Med.* 2010;104(7):925-933.

4. Waschki B, Kirsten AM, Holz O, et al. Disease Progression and Changes in Physical Activity in Patients with Chronic Obstructive Pulmonary Disease. *American journal of respiratory and critical care medicine.* 2015;192(3):295-306.

5. Bauldoff G, S.,, Hoffman L, A.,, Zullo T, G.,, Sciurba F, C. Exercise maintenance following pulmonary rehabilitation: Effect of distractive stimuli. *Chest.* 2002;122(3):948-954.

6. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med.* 1995;122:823-832.

7. Ries AL, Kaplan RM, Myers R, Prewitt LM. Maintenance after pulmonary rehabilitation in chronic lung disease: a randomized trial. *American journal of respiratory and critical care medicine.* 2003;167(6):880-888.

8. Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *The American journal of medicine.* 2000;109(3):207-212.

9. Heppner PS, Morgan C, Kaplan RM, Ries AL. Regular walking and long-term maintenance of outcomes after pulmonary rehabilitation. *Journal of cardiopulmonary rehabilitation.* 2006;26(1):44-53.

10. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. *Chest.* 2007;131(5 Suppl):4S-42S.

11. Carr SJ, Goldstein RS, Brooks D. Acute exacerbations of COPD in subjects completing pulmonary rehabilitation. *Chest.* 2007;132(1):127-134.

12. Karageorghis CI, Priest DL. Music in the exercise domain: a review and synthesis (Part I). *Int Rev Sport Exerc Psychol.* 2012;5(1):44-66.

13. Tsai HF, Chen YR, Chung MH, et al. Effectiveness of music intervention in ameliorating cancer patients' anxiety, depression, pain, and fatigue: a meta-analysis. *Cancer Nurs.* 2014;37(6):E35-50.

14. von Leupoldt A, Taube K, Schubert-Heukeshoven S, Magnussen H, Dahme B. Distractive auditory stimuli reduce the unpleasantness of dyspnea during exercise in patients with COPD. *Chest.* 2007;132(5):1506-1512.

15. Bellieni C, Cioncoloni D, Mazzanti S, et al. Music provided through a portable media player (iPod) blunts pain during physical therapy. *Pain Manag Nurs.* 2013;14(4):e151-155.

16. Thaut MH. The discovery of human auditory-motor entrainment and its role in the development of neurologic music therapy. *Prog Brain Res.* 2015;217:253-266.

17. Alter DA, O'Sullivan M, Oh PI, et al. Synchronized personalized music audio-playlists to improve adherence to physical activity among patients participating in a structured exercise program: a proof-of-principle feasibility study. *Sports medicine - open.* 2015;1(1):7.

18. Bauldoff GS. Music: More than just a melody. *Chron Respir Dis.* 2009;6(4):195-197.

19. Thaut MH. Music Therapy, Affect Modification, and Theraputic Change: Twords an intigrative model *Music Therapy Perspectives.* 1989;7:55-62.

20. Folstein MF FS, McHugh PR 'Mini-mental State'. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatry Res.* 1975;12:189-198.

21. Leow LA, Rinchon C, Grahn J. Familiarity with music increases walking speed in rhythmic auditory cuing. *Annals of the New York Academy of Sciences.* 2015;1337:53-61.

22. Leow LA, Parrott T, Grahn JA. Individual differences in beat perception affect gait responses to low- and high-groove music. *Front Hum Neurosci.* 2014;8:811.

23. Society AT. *ATS Statement: Guidelines for the Six-Minute Walk Test.* 2002.

24. Roerdink M, Bank PJ, Peper CL, Beek PJ. Walking to the beat of different drums: practical implications for the use of acoustic rhythms in gait rehabilitation. *Gait Posture.* 2011;33(4):690-694.

25. American Thoracic Society. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med.* 2002;166:111-117.

26. Belza B, Steele BG, Hunziker J, Lakshminaryan S, Holt L, Buchner DM. Correlates of Physical Activity in Chronic Obtructive Pulmonary Disease. *Nursing Research.* 2001;50(4):195-202.

27. Singh SJ, Puhan MA, Andrianopoulos V, et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. *Eur Respir J.* 2014;44(6):1447-1478.

28. Casanova C, 1.,, Cote C, G., , Marin J, M., , et al. The 6-min walking distance: long-term follow up in patients with COPD. *Europen Respiratory Journal* 2007;29(3):535-540.

29. Starobin D, Mordechai R, . K.,, Yarmolovsky A, et al. Assessment of Functional Capacity in Patients with Chronic Obstructive Pulmonary Disease- Correlation between Cardiopulmonary Exercise, 6 Minute Walk and 15 Step Exercise Oximetry Test. *Israel Medicine Association Jounal* 2006;8.

30. Kaplan RM, Atkins CJ, Reinsch S. Specific efficacy expectations mediate exercise compliance in patients with COPD. *Health Psychol.* 1984;3(3):223-242.

31. Lorig K, Stewart AL, Ritter P, Gonzalez V, Laurent D, Lynch J. *Outcome measures for health education and other health care interventions.* Thousand Oaks, CA: Sage Publications; 1996.

32. Borg G. Psychophysical Bases of Percived Exertion *Medicine and Science in Sports and Exercise* 1982;14(5):337-381.

33. Parshall MB, Schwartzstein RM, Adams L, et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *American journal of respiratory and critical care medicine.* 2012;185(4):435-452.

34. Meek PM, Lareau S. Critical Outcomes in Pulmonary Rehabilitation: Assessment and Evaluation of Dyspnea and Fatigue. *Journal of Rehabiliation Research and Development* 2003;40(5):13-24.

35. Kendrick K, Baxi S, Smith R. Usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma. *Journal of Emergency Nursing* 2000;26(3):216-222.

36. Eakin EG, Sassi-Dambron DE, Ries AL, Kaplan RM. Reliability and validity of dyspnea measures in patients with obstructive lung disease. *International Journal of Behavioral Medicine.* 1995;2(2):118-118.

37. Crisafulli E, Clini E. Measures of dyspnea in pulmonary rehabilitation Metodi per misurare la dispnea in riabilitazione respiratoria. *Multidoscoplinary Respiratory Medicine.* 2010;5(3):202-210.

38. Alvar A. ea. *Golbal Initiative for Chornic Obstructive Lung Disease.* Global Initiative for Chronic Obstructive Lung Disease, Inc.;2017.

39. Meek PM. Measurement of dyspnea in chronic obstructive pulmonary disease: what is the tool telling you? *Chronic Respiratory Disease* 2004;1:29-37.

40. Fletcher C. Standardised questionnaire on respiratory symptoms: a statement prepared and approved by the MRC Committee on the Aetiology of Chronic Bronchitis (MRC breathlessness score). *BMJ.* 1960;2:1662.

41. Meek PM, Banzett R, Parshall MB, Gracely RH, Schwartzstein RM, Lansing R. Reliability and validity of the multidimensional dyspnea profile. *Chest.* 2012;141(6):1546-1553.

42. Mahler DA, Ward J, Waterman LA, McCusker C, Zuwallack R, Baird JC. Patient-reported dyspnea in COPD reliability and association with stage of disease. *Chest.* 2009;136(6):1473-1479.

43. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax.* 1987;42:773-778.

44. Wijkstra P, J.,, TenVergert E, M.,, Van Altena R, et al. Reliability and validity of the chronic respiratory questionnaire (CRQ). *Thorax.* 1994;49:465-467.

45. Martin L, L. Validity and Reliability of a Quality- of-Life Instrument. *Clinical Nursing Research.* 1994;3(2):146-156.

46. Lacasse Y, Wong E, Guyatt G, H. A systematic overview of the measurement properties of the Chronic Respiratory Questionnaire. *Canadian Respiratory Journal.* 1997;4(3).

47. Guyatt GH. The Chronic Respiratory Questionnaire: Background information and interviewing suggestions.1986, McMaster University, Canada.

48. Waterhouse J, C., , Harper R, Marsh F, Jones N, M,B., , Brazier J, E., , Howard P. Measuring quality of life in chronic obstructive pulmonary disease. Can we assess change? *European Respiratory Journal.* 1994;419.

49. West JB, ed *Respiratory Physiology The Essentials.* Baltimore, MD: Lippincott Williams & Wilkins; 2012.

50. Lange P, Celli B, Agusti A, et al. Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease. *N Engl J Med.* 2015;373(2):111-122.

51. Hansen E, Xing-Guo S, Wasserman K. Discriminating Measures and Normal Values for Expiratory Obstruction. *Chest.* 2006;129(2):369-377.

52. Ware JEJ. http://www.qualitymetric.com/demos/SF-36v2.html. 2003. Accessed May 24, 2003, 2003.

53. Ware J., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). *Medical Care.* 1992;30(6):473-483.

54. Parshall MB, Mapel DW, Rice L, Williams A, O'Reilly J. Predictive validity of short-form health survey [36 items] scales for chronic obstructive pulmonary disease exacerbation. *Heart Lung.* 2008;37(5):356-365.

55. Ware JE, Jr. Scales for measuring general health perceptions. *Health Serv Res.* 1976;11(4):396-415.

56. Ware JE, Jr. SF-36 health survey update. *Spine (Phila Pa 1976).* 2000;25(24):3130-3139.

57. McHorney CA, Ware JE, Lu JFR, Sherbourne CD. The MOS 36-Item Short-Form Health Survey (SF-36®): III. tests of data quality, scaling assumptions and reliability across diverse patient groups. *Medical Care.* 1994;32(4):40-66.

58. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47(11):1245-1251.

59. Collins EG, Halabi S, Langston M, Schnell T, Tobin MJ, Laghi F. Sexual dysfunction in men with COPD: impact on quality of life and survival. *Lung.* 2012;190(5):545-556.

60. Halabi S, Collins EG, Thorevska N, Tobin MJ, Laghi F. Relationship between depressive symptoms and hypogonadism in men with COPD. *COPD.* 2011;8(5):346-353.

61. Groot V, Beckerman H, Lankhorts G, Bouter L, M. How to measure comorbidity: a critical review of available methods. *Joournal of Epidemilogy.* 2003;56.

62. Spielberger CD, Gorsuch RL, Luschene RE. *Manual for State-Trait Anxiety Inventory.* Palo Alto1970.

63. Kunik ME, Roundy K, Veazey C, et al. Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. *Chest.* 2005;127(4):1205-1211.

64. Okun A, Stein RE, Bauman LJ, Silver EJ. Content validity of the Psychiatric Symptom Index, CES-depression Scale, and State-Trait Anxiety Inventory from the perspective of DSM-IV. *Psychol Rep.* 1996;79(3 Pt 1):1059-1069.

65. Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. *Manual for the State-Trait Anxiety Inventory.* Palo Alto, Ca1983.

66. Kabacoff RI, Segal DL, Hersen M, van Hasselt VB. Psychometric properties and diagnostic utility of the Beck Anxiety Inventory and the State-Trait Anxiety Inventory with older adult psychiatric outpatients. *Journal Anxiety Disorders* 1997;11:33-47.

67. Barker HR, Wadsworth AP, Wilson W, . . Factor structure of the State-Trait Anxiety Inventory in a Nonstressful Situation. *Journal Clinical Psychology* 1976;32:595-598.

68. Yesavage J. A., Brink TL. Development-and-validation-of-a-geriatric-depression-screening-scale-A-preliminary-report_. *Journal of Psychiatric Research.* 1983;17(1):37-49.

69. Yesavage JA, Sheikh JI. 9/Geriatric Depression Scale (GDS). *Clinical Gerontologist.* 2008;5(1-2):165-173.

70. Greenberg S. How to try this. The Geriatric Depression Scale: Short Form: depression in older adults is underdiagnosed; try this short, simple tool to screen for depression. *American Journal Of Nursing,.* 2007;107 (10):60-69.

71. Yesavage JA, Terence LL, Huang V. Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of psychiatric research.* 1983;Volume 17 (Issue 1): 37 - 49

72. Brown LM, Schinka JA. Development and initial validation of a 15-item informant version of the Geriatric Depression Scale. *Int J Geriatr Psychiatry.* 2005;20(10):911-918.

73. Weintraub D SK, Stern MB. Effect of Age on Geriatric Depression Scale Performance in Parkinson's Disease. *Official journal of the Movement Disorder Society.* 2007;22(9):1331-1335.

74. Wittwer JE, Webster KE, Hill K. Effect of rhythmic auditory cueing on gait in people with Alzheimer disease. *Archives of physical medicine and rehabilitation.* 2013;94(4):718-724.

75. McCarten JR, Anderson P, Kuskowski MA, McPherson SE, Borson S. Screening for cognitive impairment in an elderly veteran population: acceptability and results using different versions of the Mini-Cog. *Journal of the American Geriatrics Society.* 2011;59(2):309-313.

76. Borson S, Scanlan JM, Watanabe J, Tu SP, Lessig M. Improving identification of cognitive impairment in primary care. *Int J Geriatr Psychiatry.* 2006;21(4):349-355.

77. Tombaugh TN, McIntyre, N.I. . The Mini-Mental State Examination: A Comprehensive Review. *Journal of American Geriatric Society* 1992;40:922-935.

78. Anthony JCJC. Limits of the 'Mini-Mental State' as a screening test for dementia and delirium among hospital patients. *Psychological Medicine.* 1982;12(2):397 - 408.

79. Jorm A., Scott R., J.S. C. Performance of the Informant Questionnaire on Cognitive Decline in the EIderly (IQCODE) as a Screening Test for Dementia. *Psychological Medicine* 1991;21:785-790.

80. Bronas UG, Everett S, Steffen A, et al. Rhythmic Auditory Music Stimulation Enhances Walking Distance in Patients With Claudication: A FEASIBILITY STUDY. *J Cardiopulm Rehabil Prev.* 2017.

81. Holland AE, Nici L. The return of the minimum clinically important difference for 6-minute-walk distance in chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine.* 2013;187(4):335-336.

82. Karpman C, Benzo R. Gait speed as a measure of functional status in COPD patients. *Int J Chron Obstruct Pulmon Dis.* 2014;9:1315-1320.

83. Casanova C, Celli BR, Barria P, et al. The 6-min walk distance in healthy subjects: reference standards from seven countries. *Eur Respir J.* 2011;37(1):150-156.

84. Bauldoff GS, Hoffman LA, Zullo TG, Sciurba FC. Exercise maintenance following pulmonary rehabilitation*: Effect of distractive stimuli. *Chest.* 2002;122(3):948-954.

85. Ho CF, Maa SH, Shyu YI, Lai YT, Hung TC, Chen HC. Effectiveness of paced walking to music at home for patients with COPD. *COPD.* 2012;9(5):447-457.

86. Slaght J, Senechal M, Hrubeniuk TJ, Mayo A, Bouchard DR. Walking Cadence to Exercise at Moderate Intensity for Adults: A Systematic Review. *J Sports Med (Hindawi Publ Corp).* 2017;2017:4641203.

87. Karageorghis CI, Priest DL. Music in the exercise domain: a review and synthesis (Part II). *Int Rev Sport Exerc Psychol.* 2012;5(1):67-84.

88. Brody R. Music medicine. . *Omni.* 1984;6:110–116.

89. Smoller JW PM, Ottto MW, Rosenbaum JF, Kradin RL. . State of the art: panic anxiety, dyspnea and respiratory disease. *American Journal of Respiratory Critical Care Medicine* 1996;154:6–17.

90. Gift AG MT, Soeken K. . Relaxation to reduce dyspnea and anxiety in COPD patients. *Nurs Res.* 1992;41:242–246.

91. Renfroe KL. Effect of progressive relaxation on dyspnea and state anxiety in patients with chronic obstructive pulmonary disease. . *Heart Lung* 1988;17:408–413.

92. von Leupoldt Aea. Distractive Auditory Stimuli Reduce the Unpleasantness of Dyspnea During Exercise in Patients With COPD. *CHEST.* 2007;132(5).

93. Aryal S, Diaz-Guzman E, Mannino DM. COPD and gender differences: an update. *Transl Res.* 2013;162(4):208-218.

94. Lamprecht Bea. Sex-related differences in respiratory symptoms: results from the BOLD Study. *European Respiratory Journal.* 2013(42):858–886.

95. Camp PG, O'Donnell DE, Postma DS. Chronic obstructive pulmonary disease in men and women: myths and reality. *Proceedings of the American Thoracic Society.* 2009;6(6):535-538.

96. Johnson JL, Campbell AC, Bowers M, Nichol AM. Understanding the social consequences of chronic obstructive pulmonary disease: the effects of stigma and gender. *Proceedings of the American Thoracic Society.* 2007;4(8):680-682.

97. Watson L, Vestbo J, Postma DS, et al. Gender differences in the management and experience of Chronic Obstructive Pulmonary Disease. *Respiratory medicine.* 2004;98(12):1207-1213.

98. Blakemore A, Dickens C, Guthrie E, et al. Depression and anxiety predict health-related quality of life in chronic obstructive pulmonary disease: systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis.* 2014;9:501-512.

99. Parreira VF KR, Towns M, et al. Is there an association between symptoms of anxiety and depression and quality of life in patients with chronic obstructive pulmonary disease? . Is there an association between symptoms of anxiety and depression and quality of life in patients with chronic obstructive pulmonary disease? *Canadian Respiratory Journal : Journal of the Canadian Thoracic Society.* 2015;22(1).

100. Pirraglia PA, Casserly B, Velasco R, Borgia M, L.,, Nici L. Association of change in depression and anxiety symptoms with functional outcomes in pulmonary rehabilitation patient. *Journal of Psychosomatic Research* 2011;71:45-49.

101. Punekar YS, Riley JH, Lloyd E, Driessen M, Singh SJ. Systematic review of the association between exercise tests and patient-reported outcomes in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 2017;12:2487-2506.

Table 1. Classification of Airflow Limitation According to the Global Initiative for Chronic Obstructed Lung Disease

Gold Stage	Criteria
1	Mild, $FEV_1 \geq$ 80% predicted
2	Moderate, 50% $\leq FEV_1 <$ 80% predicted
3	Severe, 30% $\leq FEV_1 <$ 50% predicted
4	Very Severe, $FEV_1 <$ 30% predicted

Table 2. Descriptive Characteristics (n=25)

Variable	Mean (SD)
Age	70.7 (4.52)
Smoking (pack years)	49.0 (31.4)
60 second step count (steps)	103.0 (7.9)
BMI (kg/m^2)	27 (4)
FEV_1/FVC (%)	47.3 (9.7)
FEV_1 % predicted	46.6 (14.8)
Charlson Co-morbidity Index	1.84 (.987)
mMRC	1.0 (.645)
Baseline Cadence (steps/min)	103 (8)
No Music 6-MWD (m)	451 (80.6)
Music 6-MWD (m)	451 (134)
RAS 6-MWD (m)	463 (71.8)
State Trait Anxiety Index-Trait	23.7 (5.15)
State Trait Anxiety Index-State	38.4 (5.84)
Geriatric Depression Scale	1.68 (2.08)
Chronic Respiratory Disease Questionnaire	
Dyspnea	20.8 (6.51)
Fatigue	19.9 (4.09)
Emotion	40.2 (7.11)
Mastery	23.7 (4.53)
Short Form 36 Physical Component Score	42.5 (7.7)
Short Form 36 Mental Component Score	56.5 (7.7)

SD=standard deviation, BMI= body mass index, mMRC= Modified Medical Research Council breathlessness scale

Table 3. Primary Outcomes: 6-Minute Walk Distance and Perceived Dyspnea (n=25)

	Mean (SD)	Mean (SD)	P value	Mean (SD)	P value	P value
Variable	NM	Music	NM-M	RAS	NM-RAS	M-RAS
6-MWD (m)	451 (81)	451 (80)	0.96	463 (72)	0.015	0.033
Dyspnea onset (m)	378 (121)	391 (134)	.543	399 (143)	.307	.576
Dyspnea peak (m)	2.7 (1.7)	2.4 (1.8)	.121	2.5 (1.6)	.317	.525

6-MWD= six-minute walking distance in meters, Dyspnea Onset= dyspnea free walk distance, Dyspnea peak= dyspnea at the end of the 6-minute walk (Modified Borg Scale of 0 to 10), NM=no music, M=music as recorded, RAS=rhythmic auditory stimulation.
scores indicate = better HrQoL**)**

Table 2. Walk Cadence During 6-MWT (n=25)

Variable	Mean (SD) NM	Mean (SD) M	P-value NM-M	Mean (SD) RAS	P-value NM-RAS	P-value M-RAS
Walking Cadence 1-2 (min)	105 (9)	108(11)	.022	110 (12)	.005	.110
Walking Cadence 3-4 (min)	107 (12)	108 (13)	.368	110 (10)	.002	.092
Walking Cadence 5-6 (min)	107 (13)	108 (13)	.367	110 (11)	.004	.003

Cadence= steps per minute recorded specified my different minute intervals during the 6-Minute Walk Test
RAS=Rhythmic Auditory Stimulation, NM= No Music

Table 3. Relationships Between Distances Walked and Selected Variables

Variable	Distance NM	Distance M	Distance RAS
FEV1 % predicted	.222	.198	.298
Pack/years smoked	-.118	-.095	-.128
Co-morbidity Score	-.039	. -.011	.007
GDS	0.13	-.016	.043
CRQ			
Dyspnea	.443*	.519**	.498*
Fatigue	271	.194	.218
Emotion	.06	-.04	-.12
Mastery	.106	.092	.058
SF36			
PCS	.172	.071	.108
MCS	-.119	-.142	-.11
Anxiety			
State	-.148	-.071	-.090
Trait	.184	.273	.223

*<.05, **<.01

NM=No Music, M= Music, RAS=Rhythmic Auditory Stimulation, Distance during 6-Minute Walk Test for walk conditions, Pack/years=smoking in pack years, Co-morbidity=Charlson Comorbidity Score (higher number=more comorbidities), GDS= Geriatric Depression Scale (score of 5 > indicate possible depression, and 7> probable depression), CRQ= Chronic Respiratory Questionnaire dyspnea domain (higher scores indicates =worse subjective experience of dyspnea in everyday life), SF-36= 36 short form health survey (PCS= physical component scale, MCS= mental component scale, higher scores indicate = better HrQL**),** Anxiety=STAI= state trait anxiety inventory (higher number= more anxiety).

Table 4. Relationships Between Onset of Dyspnea and Selected Variables

Variable	Onset Dyspnea NM	Onset Dyspnea M	Onset Dyspnea RAS
FEV1 % predicted	-.069	.277	.688
Pack/years smoked	-.067	.034	.086
Co-morbidity Score	-.097	.013	-.038
GDS	-.308	-.010	-.053
6-MWD			
NM	.450*	.706**	.667**
M	.464*	.737**	.688*
RAS	.388	.655**	.626**
CRQ			
Dyspnea	-.093	.164	.024
Fatigue	.119	.055	.080
Emotion	.264	.024	.067
Mastery	.251	-.010	.007
SF36			
PCS	.172	.071	.108
MCS	-.119	-.142	-.11
Anxiety			
State	-.245	.084	.012
Trait	-.091	.334	.181

*<.05, **<.01

NM=No Music, M= Music, RAS=Rhythmic Auditory Stimulation, Onset Dyspnea calculated in feet during 6-MinuteWalk Test for walk conditions was calculated , Pack/years=smoking in pack years, Co-morbidity=Charlson Comorbidity Score (higher number=more comorbidities), Anxiety=STAI= state trait anxiety inventory (higher number= more anxiety), GDS= Geriatric Depression Scale (score of 5 > indicate possible depression, and 7> probable depression), CRQ= Chronic Respiratory Questionnaire dyspnea domain (higher scores indicates =worse subjective experience of dyspnea in everyday life), SF-36= 36 short form health survey (higher scores indicate = better HrQL**).**

An Exploration of Sedentary Time in Individuals with COPD

Introduction

Sedentary behavior has been identified as an independent risk factor for illness, poor health outcomes and even death.[1] Efforts to quantify physical activity (PA) have led to new vantages on how PA may vary among special populations. Of different patient groups with chronic illness, patients with chronic obstructive pulmonary disease (COPD) are amongst the least active.[2] Patients with COPD are often limited by breathlessness which in turn affects their exercise capacity and functional status.[3] Reduced exercise capacity and functional status may lead to increased levels of inactivity, worsening of symptoms, deconditioning, hospitalization, and increased risk for death.[4,5,6] Understanding the relationship between sedentary behavior and clinical outcomes in this patient population is critical to improving management and therapy for patients with COPD.

Regular PA plays a critical role in the management of chronic diseases such as COPD. Maintenance and promotion of PA in patients with COPD have been associated with a reduction in hospital admissions, increased quality of live, as well as, better survival rates.[7-11] Staying physically active is an important focus for treatment of patients with COPD.[12-14] While conventional pulmonary rehabilitation is associated with small increases in physical activity in everyday life, these gains are not sustained over longer periods of time.[13]

Behaviors that influence the amount of time and reasons for increasing sedentary time (ST) in patients with COPD are poorly understood.[3,15,16] Most adults spend between 46 to 59% of their walking hours sedentary.[17,18] The mean older adult step count ranges from 4000 to 8000 steps daily.[19,20] The Sedentary Behavior Research Network defines sedentary behavior as “any waking behavior characterized by an energy expenditure of $\leq$1.5 metabolic equivalents (METS), while in a sitting, reclining or lying posture."[21] Activities such as watching television, working on a computer, talking or texting on the phone, reading, or riding in a car, bus or train constitute sedentary behaviors.[21] Over the past 10-15 years, there have been more studies focused on sedentary behavior.[22] Increased sedentary behavior is associated with the development of Type 2 diabetes mellitus and cardiovascular disease; indeed, increased sedentary behavior increases the risk of dying from cardiovascular disease by 1.5 times.[22] Additionally, it is not only the total time spent sedentary that matters, but the way in which sedentary time is accumulated is also important. Prolonged periods of sitting have been associated with increased insulin resistance and poor glycemic control[23,24] and breaking up prolonged sedentary time with periods of light, moderate or vigorous activity have been associated with biomarkers beneficial to the development or progression of chronic disease.[18]

Increased dyspnea and fatigue associated with COPD are often attributed to the increased time that patients with COPD spend sedentary. Pitta *et al.*,[9] identified that patients with COPD, when compared to healthy, older adults, spent less time walking (44±26 vs. 81±26 minutes/day) or standing (191±99 vs. 295±109 minutes/day) and more time sitting (374±139 vs. 306±18 minutes/day) and about 64% time sedentary. Coronado *et al.*, reported even higher numbers and described COPD patients spending 82% of their time sedentary.[25] In general, patients with COPD spend 57% as much time in daily physical activities as healthy older adults.[26] With less time spent physically active, patients with COPD are spending more time sedentary.

The purpose of this cross-sectional study was to investigate sedentary behavior and physical activity in patients with COPD. In addition, we examined the relationship between symptoms, function, physiologic variables and sedentary behavior in patients with COPD.

Methods

Study Sample and Design

Physical activity and sedentary time, pulmonary function, six-minute walk distance, symptoms, quality of life, self-efficacy and co-morbidities were explored in this cross-sectional study. IRB approval was obtained for the parent study from the Edward Hines Jr., VA Hospital and the University of Illinois at Chicago for this analysis.

Patients with moderate-to-severe COPD were recruited from Edward Hines Jr., VA Hospital between April and October 2017. Inclusion criteria was as follows: >40 years of age, $FEV_1/FVC < 70\%$, Mean $SpO_2 > 90\%$, $FEV_1 \leq 70\%$, and able to walk. Exclusion criteria included: respiratory infection/exacerbation within the previous four weeks, congestive heart failure (New York Heart Association Class III or IV), exercise-limiting peripheral arterial disease (stops exercise due to intermittent claudication), stops exercise due to arthritic pain in the knee or hips (self-report), Mini Mental State Exam (MMSE)[102] score ≤23, or being wheelchair bound. No participant was excluded based on gender, ethnicity or smoking status.

Patients were invited to participate via a letter or they responded to a posted flyer. After written informed consent was obtained, patients completed a six-minute walk test (6-MWT), completed questionnaires and were given the Actigraph® GT3X to wear for seven days. The patient either mailed back or physically returned the accelerometer upon completion.

Measures

Demographic and Medical Information. Pulmonary function tests were completed in the pulmonary function laboratory and were conducted according to American Thoracic Society and European Respiratory Society procedures.[27] Demographic information, the MMSE and a brief medical history were obtained. All patients scored 24 or greater on the MMSE indicating normal cognition. Body height and weight were measured using standard anthropometric procedures using a standardized scale and stadiometer.

Six Minute Walk Test. Standard testing procedures outlined by the American Thoracic Society (ATS) guidelines,[28] were used for the 6-MWT. Patients were asked to walk up and down a 100-foot-long corridor as fast as they could without running. They turned around a cone placed at each end of the walk. Patients were allowed to stop and rest if needed. Vital signs (blood pressure, heart rate, oxygenation $Sp0_2$) and perceived dyspnea using the modified Borg Scale were obtained prior to and after the 6-MWT.

Questionnaires. Patients completed the following questionnaires: Chronic Respiratory Disease Questionnaire,[27] the Rand Short-Form 36,[4] the State-Trait Anxiety Scale,[32-34] the Geriatric Depression Scale,[30-31] and the Self-Efficacy for Dyspnea[40] and Walking Scales.[41] The modified Medical Research Council Scale (mMRC)[43] and the Charlson Co-morbidity Index[48] were completed with study personnel.

Chronic Respiratory Disease Questionnaire (CRQ). The CRQ is a 20-item, disease-specific quality of life questionnaire with four dimensions: dyspnea, fatigue, emotional function, and mastery or the patient's feeling of control over the disease.[29] Each question is scored during a structured interview. Test-retest reliability and validity of the CRQ have been established.[30]

Short Form-36 Health Survey (SF-36): This is a general health-related quality of life instrument to quantify perceived physical function and mental health.[4] The SF-36 has two component scales, physical and mental health and eight subscales (physical function, role physical, role emotional, mental health, vitality, body pain, social function and general health. The SF-36 has established validity and reliability.[31] The physical and mental health component scores were used in this analysis.

Depression and Anxiety. The Geriatric Depression Scale[32,33] and the State-Trait Anxiety Inventory[34-36] were used to measure depressive symptoms and anxiety. Both measures have established validity and reliability.[37 38-41]

Self-Efficacy. The Self-Efficacy for Walking[42] and the Self-Efficacy for Shortness of Breath questionnaires[43] were used to measure self-efficacy. These instruments were designed to assess a patient's confidence in keeping shortness of breath from interfering from walking or from doing what they want to do and have established validity and reliability.[42, 44]

Modified Medical Research Council Scale (mMRC). The mMRC is an standard measure used for assessing secondary response to dyspnea.[45] Individuals are assigned to one of five grades. A one-unit change indicates a change in disability; a lower number indicates less dyspnea with physical activity. The mMRC has been used to categorize levels of disability from dyspnea in patients in pulmonary rehabilitation.[45-48] The mMRC has established validity and reliability.[45,349]

Charlson Comorbidity Index. This validated and widely utilized index will be used to determine whether comorbidities influence study outcomes.[50]

BODE Index. The BODE Index is a calculated score to predict mortality in patients with COPD.[51] The index is comprised of body-mass index (B), airflow obstruction as measured by the FEV1 (O), dyspnea as measured by the mMRC (D), and exercise capacity (E) as measured by the six-minute walk distance. Points for each measure are computed and an index is derived. Scores indicate the percent likelihood of 4-year survival: 0-2 =80%, 3-4 = 67% 5-6 = 57% and 7-10 = 18%.

Physical Activity and Sedentary Time. Physical activity and sedentary time were objectively measured using the Actigraph® GT3X triaxial accelerometer. The Actigraph®

GT3X is lightweight (27 grams) and worn at the waistline on the right hip and is able to record over seven consecutive days of physical activity without needing re-charging. This monitor reliably detects sedentary bouts and is preprogramed to collect continuous data in one-minute epochs (i.e. 60 seconds).[52] The Freedson [53] adult counts per minute cut points were used to define sedentary (0-99), light activity (100-759), moderate (1952-5724), and vigorous (5725-9498). This device is considered a valid and reliable tool for physical activity assessment in adults[52] and those with COPD.[54] It has acceptable test-retest reliability ([rho] (95% CI) = 0.52 (0.27-0.70)) and validity ([rho] (95% CI) = 0.30 (0.02-0.54)) for total sedentary time in older adutls.[55] Each individual accelerometer was fully charged and was pre-programmed with patients height weight, and age.

Instructions and placement of Actigraph® GT3X were given to the patients once the study questionnaires and 6-MWT were completed. Patients were instructed to wear the device on the right hip with the bevel side up for 7 consecutive days during waking hours (i.e. they did not wear it at night and removed it for bathing). At the end of the 7 days, patients returned the device in person or used a pre-paid mailing envelope.

When the accelerometer was returned, the data were extracted for analysis. Individual days of wear were screened using ActiLife® software version 6.13.3. Any 24-hour day recording without data was identified as an interruption of wear time and was filtered out. Daily waking wear hours were defined for all participants as anytime between 6:00 am to 11:59 pm. This span of time was chosen given that 80% of the patients were retired and reported variable wake time hours. Days with recordings of 10 hours or more constituted a valid day.[3] Five days[3] of valid wear data were used for analysis. The first day (when given to participant) and last day (when returned) were excluded. Non-wear time was defined as 60-minute periods of zero counts with no Kcals or step counts associated with the period.[3] Cleaned data were exported to an Excel spreadsheet for further processing. Diurnal sedentary time (ST) in minutes and bouts of ST for each day were extracted and calculated by averaging data across all valid hours. Finally, overall average ST per hour for the 5 days of wear was calculated for each participant and used in the final analysis.[56] For the final analysis, no differentiation was made between week and weekend days as 80% of our sample was retired and did not work. As such, the weekend vs weekday effect are thought to not likely be a factor in older patient populations.[3]

The Actigraph® GT3X firmware translates raw acceleration data into summary metrics of energy expenditure by using a pre-determined algorithm that is propriety to the manufacturer. The accelerometer derived metrics explored in this study included: sedentary time (in minutes per hour), percent of time per hour spent in sedentary, light, moderate, or vigorous activity, total time of sedentary bouts occurring in an hour (in minutes), number of sedentary breaks in an hour, and average steps count (in an hour). The fragmentation index [57] was also calculated. The fragmentation index is the ratio of total sedentary bouts divided by the sedentary time for each participant. The fragmentation index is a measure of behavior dynamics that can help summarize patterns of how the sedentary time is accumulated into a single number.[3,15,57] A higher fragmentation index reflects that the sedentary time was accumulated in shorter bouts i.e. fragmented versus longer periods of sitting with no breaks.

Statistical Analysis

SPSS version 25 was used for all statistical analysis. Data were tested for normality using the Kolmogorov-Smirnov and Shapiro-Wilks tests. FEV_1 percent predicted, 6-MWT distance, and fragmentation index were normally distributed ($p > .05$). Descriptive statistics (mean, standard deviation) were used to describe the sample and results. Pearson r correlations were used to explore relationships between study variables and sedentary time.

Results

Twenty-five older, adult men (age = 70.7 ± 4.5 yr) with moderate-to-severe COPD (FEV_1 = 47.4 ± 9.7% predicted) were enrolled. The sample consisted of 17 whites and 4 African Americans. Average pack years reported was 47.8 ± 28.4. There were 5 current smokers in the sample. A total of five patients reported using home oxygen of which only one participant used supplemental oxygen during the six-minute walk. Four participants did not return the Actigraph® GT3X, and were excluded from the final analysis *(see Table 7)*. Once the data were cleaned to fit the criteria for valid wear time, four participants were identified to have less than 5 days of valid wear time. Of the four, two had 4 days of valid wear time and two had 3 days of valid wear time. Evidence from the literature, from other cross- sectional studies examining accelerometer data in COPD patients over 5 days, determined that two days constituted valid wear time to sufficiently characterize free-living PA.[3] Additionally, there were no differences in major demographic variables and sedentary time between these four patients and the remaining 17 patients. For this reason, we included these four participants (*n*= 21) in our final analysis. There were no adverse events related to the study procedures.

Demographic information, descriptive statistics for the accelerometer metrics and subjective study measures are reported in *Table 7*. Patients spent 44 minutes of each hour recorded in ST (73.9 ± 9.3%). On average, the patients spent 15 minutes (24.6 ± 9.2%) of each hour recorded in light activity, 1 minute (1.4 ± 1.2%) in moderate activity and no time in vigorous activity. The mean step count for any given hour the accelerometer was worn was 292 ± 108 steps. The mean fragmentation index was .04 ± .005.

There was a moderate, negative relationship between FEV_1 percent predicted and ST (r= -.45, p= .042). There was a positive relationship between percent sedentary time and the BODE Index (r=.45, p=.04). Small to moderate relationships were identified between the percent time spent in moderate physical activity and FEV_1 percent predicted (r=.50, p=.02), the six-minute walk distance (r=.46, p=.038), confidence in the ability to walk 2 miles (r=.51, p=.018) and the BODE Index (-.48, p=.026). There was a moderately high association identified between the fragmentation index and perceived dyspnea after the six-minute walk (r=.59, p=.005). Although not significant, there was a trend developing between dyspnea self-efficacy and the fragmentation index (r =.38, p=.09).

There were no differences in sedentary time or the fragmentation index amongst smokers versus non-smokers (p=.052; p=.61) , depressed or not depressed (p=.26; p=.15), by BMI category (p=.18; p=.68) or by COPD Gold status (p=.53; p=.86).

Discussion

The principal findings of this study follow. First, older adult veterans with COPD spend large amounts of their waking hours sedentary. Additionally, the patient's perception of dyspnea immediately following their 6MWT was significantly associated with the fragmentation index. Better lung function (increased FEV_1 percent predicted) was associated with decreases in ST. Next, a higher BODE Index (more dyspnea with physical activity) was associated with increased sedentary time. An increase in time spent in moderate activity was associated with better lung function, higher self-efficacy for dyspnea and increased six-minute walk distance. There were no associations between anxiety, depression, self-efficacy, quality of life and ST. Lastly, there were no differences in ST or percent time spent in light, moderate or vigorous activities between current smokers and non-smokers or based on BMI or COPD GOLD status.

Patients with COPD are more sedentary than similar aged, healthy, older adults.[18] This group was sedentary 74% of each hour. Healthy older adults are sedentary 57% percent of the time.[23] These results are consistent with other reports on ST in patients with COPD. Pitta, *et al.* reports that patients with COPD were sedentary 64% of the time.[14] Coronado, *et al.* reported that patients with COPD spent 82% of their time lying or sitting.[25] While some level of over and under estimation has been found with the accelerometer derived data, these devices provide useful estimates of ST in this the older adult patient population.[18] We did not collect measures of self- reported sedentary time or activities in free living over the 7 days. Our results provide further evidence that patients with COPD spend a great deal of their time sedentary.

Consensus on what constitutes too long of a sedentary bout for patients with COPD is still being investigated.[3] However, it is important to note that longer bouts of sedentary time that are not broken by periods of activity, have been associated with deterioration in metabolic, cardiac, and motoric health in the general population.[15] Chastin, *et al.* reported that in healthy older adults, ST tends to be accumulated in longer bouts and is associated with adiposity, muscle quality, and different activity intensity phenotypes.[57] To further quantify this finding, we calculated that the average fragmentation index was 0.04. A fragmentation index of 0.04 is low and suggests that this cohort was accumulating sedentary time in long bouts that were not often broken up by periods of physical activity. Our results, therefore, support the notion that not only are older veterans with moderate-to-severe COPD highly sedentary in their daily life, but they are also accumulating ST in ways that may be more detrimental to their physical health (i.e. of declining or worsening their cardiovascular, metabolic and motoric health).[15] Discretionary postural changes, such as sitting, standing or laying may be important outcome measures to consider in activity-compromised patients.[14,58] For example, Carlson, *et al.* reported that including 10 ST bout breaks per day resulted in an improvement of waist circumference, blood pressure, HDL, triglycerides, fasting glucose and insulin in adults.[59] These findings highlight the importance of developing adequate clinical interventions that specifically identify those individuals at higher risk for prolonged ST while finding ways to promote sedentary behavior change. Byrom, *et al*. suggested, that while using a fragmentation index has the potential to help summarize and characterize sedentary bouts, it is still unclear how many bouts is needed to generate reliable estimates by individuals.[3] More needs to be understood about how best to use and apply the index and its clinical implications. Exploring what other health outcome measures are associated with the index are needed to make more meaningful assessment of its implications.[3]

Another finding was that Borg dyspnea score immediately following the 6-MWT was positively associated with increases in fragmentation index (Figure 1). Thus, a higher level of dyspnea was associated with increases in fragmentation (higher index is better). At face value, this finding could indicate that patients who break up their sedentary time get more short-of-breath with physical activity. However, it may also suggest that those patients reporting higher levels of dyspnea[60,61] are not as limited or afraid of being breathless and may be breaking up their sedentary bouts more often. The latter may be the case since there was a weak association between distances walked and perceived dyspnea after the 6-MWT indicating that those who pushed harder had more dyspnea. Interrupting ST with activity (light or moderate), has been associated with beneficial biomarkers for chronic disease[18]; while prolonged periods of sitting have been associated with insulin resistance and poor glycemic control.[16,23]

Next, a higher BODE Index was associated with increased sedentary time. The BODE Index is a composite index comprised of BMI, degree of obstruction, dyspnea and six-minute walk distance. As the BODE Index increases, mortality also increases.[51] Interestingly, neither the BMI, mMRC nor 6-MWT distances alone had significant associations with ST. Although, there was no significant relationship identified with these individual variables and sedentary time, taken together as an index, there is a moderate relationship. Although we have no direct data to indicate that increased ST increases mortality in patients with COPD, it is reasonable to surmise that if increases in the BODE Index are associated with increased mortality and increased sedentary time is associated with the BODE Index, it may be that increased sedentary time in patients with COPD is also associated with increased mortality. The BODE Index has been shown to be related to physical activity[62] but, to our knowledge, not to sedentary behavior. It is important to note however that our sample was characterized with BODE scores in the first two categories (80% and 67% survival respectively). No patients were categorized in the higher risk categories (57% and 18% survival categories). There is no reason to believe however that an increased sedentary lifestyle would not be predictive of mortality in this population as it has been in other large cohorts of men.[63]

Our sample engaged in very little moderate PA. However, moderate PA was positively associated with FEV_1, 6-MWD, and self- efficacy for walking 2 miles without stopping. Similar results were previously reported by Steele, *et al.* who found significant correlation between accelerometer measured daily activity and 6-MWT ($r= 0.60$, $p= <0.001$), FEV_1 ($r=0.37$, $p= <0.001$), self-efficacy($r=0.27$, $p=<0.05$) and physical health status sub-scale of the SF-36 ($r= 0.40$, $p<0.01$).[64] Pitta, *et al.* reported that 6-MWD was the strongest correlate of walking time during daily life in individuals with COPD ($r=0.38$, $p=.006$).[14] These results suggest that those individuals with better lung function (increased FEV_1), greater 6-MWD, and who believe they could walk for two miles at a moderate pace without stopping spend increased time in moderate

PA. Our findings provide further support the use of accelerometer-derived data to capture moderate activity in COPD.[65,66] In practice, integrative methods that account for both pulmonary and extra pulmonary parameters (i.e. 6-MWT) may be better indicators of moderate PA in activity-compromised patients.[13,14,67,68]

The intensity of activity and not just the time spent in it are important in understanding functional capacity and those at higher risk of poor health outcomes.[65,68] In our study we found a negative association between the BODE index and moderate PA. As the BODE Index increased (less chance of survival within 4 years), moderate PA decreased. Functional status in COPD is related to walking time and intensity and can be used to predict those at higher risk of poor outcomes (BODE index ≥ 6).[60] Jehn, *et al.* reported that GOLD stage 2 COPD patients reached had low walking times and intensity (64 $\pm$ 33.2 min/day; 3.92 $\pm$7.9 min/ day).[60] Our study further exemplifies these low numbers as participants on average every hour were recording < 1 min of moderate PA. Although our results support previous findings, given that the patients in our study accumulated very low levels of moderate activity time, our results need to be interpreted with caution.

Anxiety, depression, quality of life and self-efficacy were not related to ST or the fragmentation index. The lack of significant relationships may indicate that there is no relationship between these variables and ST or the fragmentation index or it may be a result of a Type II error due to the small sample size.

Lastly, there were no differences in percent time spent sedentary or in light, moderate or vigorous physical activity between current smokers vs. non-smokers, BMI category or COPD GOLD stage. It may be that this sample was relatively homogeneous. There were only 5 current smokers, no participants in the underweight category; nine in the normal weight category, nine in the overweight category and 4 in the obese category. Likewise, most patients fell into GOLD Stage 2 and 3. As such, there may not be enough variability in a relatively small sample to highlight differences that may or may not exist.

Strengths and Limitations

The present study has various strengths and limitations. To our knowledge this is the first study attempting to explore ST in veteran older adults with COPD through the use of accelerometer data. Some of our non-significant findings may be attributed to our small and homogenous sample size. Accelerometers have become a valuable and valid tool to characterize patterns of physical activity (PA) in various patient populations. Accelerometers vary in their sensitivity to identify slower walking speeds (patients with COPD walk up to 25% slower than healthy older adults)[14], discrete positional changes and overestimate or underestimate metabolic cut points for levels of energy expenditure (i.e. light moderate, vigorous and very vigorous activity).[2,3] Thus, estimating sedentary behavior by counts of low levels of energy expenditure used for the general adult population alone can lead to misinterpretation of PA and ST accelerometer data in this patient population.[65,69,70] Mounting evidence suggests that only examining counts of energy spent sedentary may not provide sufficient insight to the factors that contribute to a sedentary lifestyle in special populations like COPD.[2,3,58] Thus, distinguishing between light and sedentary activity as well as exploring other physiological and psychological factors is critical to understanding sedentary behavior in special populations.

Historically, 60 second epochs have been used in studies examining older adults but in recent times there have been questions regarding best practice for accelerometer data cut points to capture ST in activity- compromised patient populations.[71] Atkin, et al suggested that 15 second epochs (versus the traditional 60 sec) are best suited to capture ST in older, activity-compromised patient populations.[72] Using shorter epochs may have provided more robust data for this study.

How ST is accumulated and how often those bouts are broken by activity remains an important question under investigation. One limitation of our study is that we did not collect any self-reported measures from patients during the 7 days of PA, ST, sleep as well as, time accelerometer was worn. Collecting valid self-reported measures would have allowed us to further investigate behaviors surrounding ST (e.g. TV watching) and compare these reports with the accelerometer data.[72] Having data from both the accelerometer and self-report can also help clarify any inconsistencies in the raw data. In future studies, we recommend incorporating a self-reported measure alongside the accelerometer wear time. Conversely, in our study, we were able better characterize total ST by calculating the fragmentation index. While this metric is a new way to report ST data, it shows promise in summarizing total ST and number of bouts broken into one number.[15]

Not finding significant relationships amongst psychological factors and ST may have been a product of being underpowered as well as having a homogenous sample of all men with relatively similar severity of disease. We hypothesized that there may be more discrete variability in the way the psychological factors may present in everyday life for this population, which may have not been captured at the baseline, and because we did not include a self-report measure over those 7 days. Future studies may want to include self-reported measures that can capture psychological factor variability, throughout the 7 days of wear. Additionally, larger studies with a more diversified patient population may help reveal how psychological factors relate to ST.

We intended to include predictive modeling for ST in our report. Given that the FEV_1 percent predicted and BODE index were the only two parameters that were related to ST in a bivariate analysis, and that the FEV_1 percent predicted composes part of the BODE index, we did not include predictive modeling in this report. Predictive modeling should be included in future studies that are sufficiently powered.

Placement of the accelerometer plays a role in motion sensor detection. While wearing the Actigraph® GT3X on the hip is considered a standard placement to capture free-living PA, this location does present some limitations in the slower walking speeds. Reduced speed and subtle postural changes may not have been captured by the placement of the Actigraph® GT3X on the hip. Distinguishing between these postures and detecting slower speeds may be important to accurately characterize free-living PA and ST in activity-compromised patient populations.[3] To date, only the ActivPAL (PAL Technologies, Glasgow, UK) is worn on the thigh and have the sensitivity to detect postural changes.

Conclusion

Older adult veteran patients with COPD display high levels of ST that are accumulated in larger bouts of time. The BODE index was associated with increased ST, which may suggest that patients with higher BODE scores spend more time sedentary and have a decreased chance of survival. FEV_1, higher self-efficacy for dyspnea and increased 6-MWT were associated with increase time spent in moderate activity Taken together, these results emphasize the complexity of sedentary behavior in COPD patients which is most likely affected by an interaction of both physical (pulmonary) and psychological factors. Further research in larger more varied cohorts of COPD patients is needed to understand what specific factors contribute and predict to ST and how this may be addressed in the clinical setting.

References

1. Chastin SF, Granat MH. Methods for objective measure, quantification and analysis of sedentary behaviour and inactivity. *Gait Posture.* 2010;31(1):82-86.

2. Tudor-Locke CR, D.A.;. Using Cadence to Study Free-Living Ambulatory Behaviour. *Sports Med.* 2012;42(5):381-398.

3. Byrom B, Rowe DA. Measuring free-living physical activity in COPD patients: Deriving methodology standards for clinical trials through a review of research studies. *Contemp Clin Trials.* 2016;47:172-184.

4. Ries AL, Bauldoff GS, Carlin BW, et al. Pulmonary Rehabilitation: Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines. *Chest.* 2007;131(5 Suppl):4S-42S.

5. Carr SJ, Goldstein RS, Brooks D. Acute exacerbations of COPD in subjects completing pulmonary rehabilitation. *Chest.* 2007;132(1):127-134.

6. Waschki B, Kirsten AM, Holz O, et al. Disease Progression and Changes in Physical Activity in Patients with Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med.* 2015;192(3):295-306.

7. van Gestel AJ CC, Sto¨whas AC, Rossi VA, Sievi NA, Camen G, Russi EW, Kohler M. . Predicting daily physical activity in patients with chronic obstructive pulmonary disease. *PLoS One.* 2012;7(e48081).

8. Agarwal V, Tetenta S, Bautista J, ZuWallack R, Lahiri BL. Longitudinal changes in directly measured physical activity in patients with chronic obstructive pulmonary disease: the trajectory of change. *J Cardiopulm Rehabil Prev.* 2012;32:292–295.

9. Pitta F TT, Spruit MA, Probst VS, Decramer M, Gosselink R. 171. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2005;171:972–977.

10. Waschki B SM, Watz H, Albert PS, Shrikrishna D, Groenen M, Smith, C MW, Tal-Singer R, Edwards LD, et al. . Physical activity monitoring in COPD: compliance and associations with clinical characteristics in a multicenter study. *Respir Med.* 2012;106:522–530.

11. Watz H WB, Meyer T, Magnussen H. Physical activity in patients with COPD. *Eur Respir J.* 2009;33:262–272.

12. Mesquita R, Meijer K, Pitta F, et al. Changes in physical activity and sedentary behaviour following pulmonary rehabilitation in patients with COPD. *Respir Med.* 2017;126:122-129.

13. Pitta F, Troosters T, Probst VS, Langer D, Decramer M, Gosselink R. Are patients with COPD more active after pulmonary rehabilitation? *Chest.* 2008;134(2):273-280.

14. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2005;171(9):972-977.

15. Tieges Z, Mead G, Allerhand M, et al. Sedentary behavior in the first year after stroke: a longitudinal cohort study with objective measures. *Arch Phys Med Rehabil.* 2015;96(1):15-23.

16. Hill K, Gardiner PA, Cavalheri V, Jenkins SC, Healy GN. Physical activity and sedentary behaviour: applying lessons to chronic obstructive pulmonary disease. *Intern Med J.* 2015;45(5):474-482.

17. Owen N SJ, Koohsari MJ, et al. Sedentary behavior and health: mapping environmental and social contexts to underpin chronic disease prevention. *Br J Sports Med.* 2014;48:174-177.

18. Healy GN, Clark BK, Winkler EA, Gardiner PA, Brown WJ, Matthews CE. Measurement of adults' sedentary time in population-based studies. *Am J Prev Med.* 2011;41(2):216-227.

19. Chan CS, Slaughter SE, Jones CA, Ickert C, Wagg AS. Measuring Activity Performance of Older Adults Using the activPAL: A Rapid Review. *Healthcare (Basel).* 2017;5:4.

20. Slaght J, Senechal M, Hrubeniuk TJ, Mayo A, Bouchard DR. Walking Cadence to Exercise at Moderate Intensity for Adults: A Systematic Review. *J Sports Med* 2017;2017:4641203.

21. Tremblay MS, Aubert, S., Barnes, J.D., Saunders, T.J., Carson V., Latimer-Cheung, A,E., Chastin, S.F.M., Altenburg, T.M., Chinapaw, M.J.M. SBRN Terminology Consensus Project Participants. Sedentary Behavior Research Network (SBRN) – Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act.* 2017;10(14):75.

22. Wilmot EG, Edwardson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. *Diabetologia.* 2012;55(11):2895-2905.

23. Buckley JP MD, Morris M, et. al ., Standing-based office work shows encouraging signs of attenuating post-prandial glycaemic excursion. *Occup Environ Med.* 2014;71:109-111.

24. Dunstan DW KB, Larsen R, Healy GN, Cerin E, Hamilton MT, Shaw JE, Bertovic DA, Zimmet PZ, Salmon J, Owen N. Breaking up prolonged sitting reduces postprandial glucose and insulin responses. *Diabetes Care*. 2012;35:976-983.

25. Coronado M JJ, de MB, Terrier P, Schuttz Y, Fitting JW. Walking activity measured by accelerometry during respiratory rehabilitation. *Cardiopulm Rehabil.* 2003;23:357-364.

26. Vorrink SNW KH, Troosters T, Lammers JJ. Level of daily physical activity in individuals with COPD compared with healthy controls. *Respir Res.* 2011;12:33.

27. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J.* 2005;26(2):319-338.

28. American Thoracic Society. ATS Statement: Guidelines for the Six-Minute Walk Test. *Am J Respir Crit Care Med.* 2002;166:111-117.

29. Guyatt G, Berman, L, Townsend, S, Pugsley, S, Chambers, L. . Long-term outcome after respiratory rehabilitation. Canadian Medical Association Journal. *Can Med Assoc J.* 1987;137(1089–1095.).

30. Lacasse Y, Wong, E, Guyatt, G.H, King, D, Cook, D.J, Goldstein, R.S. . Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *The Lancet.* 1996;348:1115–1119.

31. McHorney C, Ware, J., Lu, J. and Sherbourne, C. The MOS 36-item short-form health survey (SF-36). Tests of data quality, scaling assumptions and reliability across diverse patient groups. *Med Care.* 1994;32:40-66.

32. Yesavage J. A., Brink TL. Development-and-validation-of-a-geriatric-depression-screening-scale-A-preliminary-report. *J Psych Res.* 1983;17(1):37-49.

33. Yesavage JA, Sheikh JI. 9/Geriatric Depression Scale (GDS). *Clinl Gerontol.* 2008;5(1-2):165-173.

34. Spielberger CD, Gorsuch RL, Luschene RE. *Manual for State-Trait Anxiety Inventory.* Palo Alto, 1970.

35. Kunik ME, Roundy K, Veazey C, et al. Surprisingly high prevalence of anxiety and depression in chronic breathing disorders. *Chest.* 2005;127(4):1205-1211.

36. Okun A, Stein RE, Bauman LJ, Silver EJ. Content validity of the Psychiatric Symptom Index, CES-depression Scale, and State-Trait Anxiety Inventory from the perspective of DSM-IV. *Psychol Rep.* 1996;79(3 Pt 1):1059-1069.

37. Kabacoff RI, Segal DL, Hersen M, van Hasselt VB. Psychometric properties and diagnostic utility of the Beck Anxiety Inventory and the State-Trait Anxiety Inventory with older adult psychiatric outpatients. *J Anx Dis.* 1997;11:33-47.

38. Barker HR, Wadsworth AP, Wilson W. Factor structure of the State-Trait Anxiety Inventory in a Nonstressful Situation. *J Clinl Psychol.* 1976;32:595-598.

39. Yesavage JA, Terence LL, Huang V. Development and validation of a geriatric depression screening scale: A preliminary report. *J Psychiatric Res.* 1983;Volume 17 (Issue 1): 37-49.

40. Brown LM, Schinka JA. Development and initial validation of a 15-item informant version of the Geriatric Depression Scale. *Int J Geriatr Psychiatry.* 2005;20(10):911-918.

41. Weintraub D SK, Stern MB. Effect of Age on Geriatric Depression Scale Performance in Parkinson's Disease. *Official Journal of the Movement Disorder Society.* 2007;22(9):1331-1335.

42. Kaplan RM, Atkins CJ, Reinsch S. Specific efficacy expectations mediate exercise compliance in patients with COPD. *Health Psychol.* 1984;3(3):223-242.

43. Lorig K, Stewart AL, Ritter P, Gonzalez V, Laurent D, Lynch J. *Outcome Measures for Health Education and Other Health Care Interventions.* Thousand Oaks, CA: Sage Publications; 1996.

44. Lorig K, Stewart A, L, Ritter P, Gonzalez V, Laurent D, L. *Outcome Measures for Health Education and Other Health Care Interventions.* Thougsand Oaks, Californa Sage; 1996.

45. Meek PM. Measurement of dyspnea in chronic obstructive pulmonary disease: what is the tool telling you? *Chron Respir Dis*. 2004;1:29-37.

46. Meek PM, Lareau S. Critical Outcomes in Pulmonary Rehabilitation: Assessment and Evaluation of Dyspnea and Fatigue. *J Rehabil Res Devel.* 2003;40(5):13-24.

47. Meek PM, Banzett R, Parshall MB, Gracely RH, Schwartzstein RM, Lansing R. Reliability and validity of the multidimensional dyspnea profile. *Chest.* 2012;141(6):1546-1553.

48. Parshall MB, Schwartzstein RM, Adams L, et al. An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med.* 2012;185(4):435-452.

49. Mahler DA, Ward J, Waterman LA, McCusker C, Zuwallack R, Baird JC. Patient-reported dyspnea in COPD reliability and association with stage of disease. *Chest.* 2009;136(6):1473-1479.

50. Charlson Mea. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47(11):1245 - 1125.

51. Bartolome R. Celli MD, Claudia G. Cote, M.D., Jose M. Marin, M.D., Ciro Casanova, M.D., Maria Montes de Oca, M.D., Reina A. Mendez, M.D., Victor Pinto Plata, M.D., and Howard J. Cabral, Ph.D. The Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index in Chronic Obstructive Pulmonary Disease. *N Engl J Med.* 2004;350:1005-1012.

52. Aadland E, Ylvisaker E. Reliability of the Actigraph GT3X+ Accelerometer in Adults under Free-Living Conditions. *PLoS One.* 2015;10(8):e0134606.

53. Freedson PSM, E; Sirard, J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Med Sci Sports Exerc.* 1998;30(5):777-781.

54. Van Remoortel H, Raste Y, Louvaris Z, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS One.* 2012;7(6):e39198.

55. Gardiner PA, Clark BK, Healy GN, Eakin EG, Winkler EA, Owen N. Measuring Older Adults' Sedentary Time- Reliability, Validity, and Responsiveness. *Med Sci Sports Exerc.* 2011;43(11):2127-2133.

56. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? *Intern J Behavior Nutr Phys Act.* 2011;8(1):62.

57. Chastin SFM, Ferriolli E, Stephens NA, Fearon KCH, Greig C. Relationship between sedentary behaviour, physical activity, muscle quality and body composition in healthy older adults. *Age and Ageing.* 2012;41(1):111-114.

58. Cohen MDC, M; . A Novel Apprach to Measuring Activity in Chronic Obstuctive Pulmonary Disease. *J Cardiopul Rehabil Prev.* 2010;30:186-194.

59. Carson V, Wong SL, Winkler E, Healy GN, Colley RC, Tremblay MS. Patterns of sedentary time and cardiometabolic risk among Canadian adults. *Prev Med.* 2014;65:23-27.

60. Jehn M, Schmidt-Trucksass A, Meyer A, Schindler C, Tamm M, Stolz D. Association of daily physical activity volume and intensity with COPD severity. *Respir Med.* 2011;105(12):1846-1852.

61. Janssens T, De Peuter S, Stans L, et al. Dyspnea Perception in COPD. *Chest.* 2011;140(3):618-625.

62. Mantoani LC H, NA, Guimaraes MM, Vitorasso RL, Probst VS, Pitta F. Does the BODE index reflect the level of physical activity in daily life in patients with COPD? *Revista Brasileria de Fisioterapia.* 2011;15(2):131-137.

63. Warren TY BV, Hooker SP, Sui X, Church TS, et al. Sedentary behaviors increase risk of cardiovascular disease mortality in men. *Med Sci Sports Exerc.* 2010;42:879-885.

64. Steele BG1 BB, Cain K, Warms C, Coppersmith J, Howard J. Bodies in motion: Monitoring daily activity and exercise with motion sensors in people with chronic pulmonary disease. *J Rehabil Res Devel.* 2003;40(5):45-58.

65. Pitta F, Troosters T, Probst VS, Spruit MA, Decramer M, Gosselink R. Quantifying physical activity in daily life with questionnaires and motion sensors in COPD. *Eur Respir J.* 2006;27(5):1040-1055.

66. Kochersberger GM, E.; Maragatha, MN.; Kuchibhatla.; Pieper, C.; . The Reliability, Validity, and Stability of a Measure of Physical Activity in the Elderly. *American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilittion.* 1996;77:793-395.

67. Nguyen HQ, Steele BG, Dougherty CM, Burr RL. Physical activity patterns of patients with cardiopulmonary illnesses. *Arch Phys Med Rehabil.* 2012;93(12):2360-2366.

68. Spruit MA, Watkins ML, Edwards LD, et al. Determinants of poor 6-min walking distance in patients with COPD: The ECLIPSE cohort. *Respir Med.* 2010;104(6):849-857.

69. Steele BG, Belza B, Cain KC, et al. A randomized clinical trial of an activity and exercise adherence intervention in chronic pulmonary disease. *Arch Phys Med Rehabil.*. 2008;89(3):404-412.

70. Steele BG, Holt L, Belza B, Ferris S, Lakshminaryan S, Buchner DM. Quantitating Physical Activity in COPD Using a Triaxial Accelerometer. *Chest.* 2000;117(5):1359-1367.

71. Edwardson CL1 GT. Epoch length and its effect on physical activity intensity. *Med Sci Sports Exerc* 2010;45(5):928-934.

72. Andrew J Atkin TG, Stacy A Clemes, Thomas Yates, Charlotte Edwardson, Soren Brage, Jo Salmon, Simon J Marshall, Stuart JH Biddle; . Methods of Measurement in epidemiology: Sedentary Behaviour, *Intern J Epidemiol*. 2012;41(5):1460–1471.

Table 7. *Sample Characteristics* (n=21)

Variable	Mean (SD)
Age (yr)	71.4 (4.0)
Race (n/%)	
White	17/ 80%
Black	4 / 20%
Height (cm)	176.2 (4.5)
Weight (kg)	81.3 (9.6)
BMI (kg/m^2)	26.2 (2.7)
BMI Categories (n/%)	
Normal weight	9 / 43%
Overweight	9 / 43%
Obese	3 / 14%
FEV_1 (L)	1.4 (.50)
FEV_1 percent predicted (%)	46.8 (15.0)
FEV_1/FVC (%)	46.2 (9.3)
Home oxygen use (n/%)	6/24%
Charlson Co-morbidity Score	2 (1.0)
Current Smokers (n and % yes)	5 (24%)
Smoking Pack Years	44.8 (28.4)
COPD GOLD Stage (n/%)	
Stage 1	1 / 5%
Stage 2	11 / 52%
Stage 3	8 / 38%
Stage 4	1 / 5%
BODE Index	1.5 (1.2)

SD=standard deviation

Table 8. Descriptive Information on Study Measures

Variable	Mean (SD)
Six-minute walk distance (m)	461.0 (71.2)
Dyspnea rating post 6MWT	2.5 (1.3)
mMRC (range=0-4)	1.0 (.7)
GDS (range=1-10)	1.6 (2.0)
Self-Efficacy Walking (%, range=0-100)	
Walk 1 block	100.0 (0)
Walk 2 blocks	96.7 (9.1)
Walk 3 blocks	92.4 (15.5)
Walk 4 blocks	88.1 (21.1)
Walk 5 blocks	83.8 (28.9)
Walk 1 mile	80.0 (33.8)
Walk 2 miles	64.8 (38.7)
Walk 3 miles	55.7 (43.1)
Self-Efficacy Dyspnea (range 0-10)	7.9 (2.5)
CRQ	
Dyspnea (range=5-35)	21.1 (6.1)
Fatigue (range=4-28)	20.0 (3.9)
Emotion (range=7-49)	41.3 (6.4)
Mastery (range=4-28)	24.6 (4.0)
SF36 (range = 0-100)	
PCS	43.6 (7.9)
MCS	56.7 (7.1)
State Trait Anxiety Index	
State	22.7 (3.7)
Trait	27.9 (5.2)
Sedentary Time (min/hr)	44.4 (5.6)
Sedentary Bouts (min/hr)	29.7 (7.4)
% Time sedentary/hr	74% (9.3)
% Time in light activity/hr	24.6% (9.23)
% Time in moderate activity/hr	1.38% (1.2)
% Time in vigorous activity/hr	0 (0)
Fragmentation Index	.04 (.005)
Steps count/hour	292 (108)

Range=possible range of instrument, SD=standard deviation, mMRC= Modified medical Research council breathless scale (higher numbers indicate worse condition), Self Efficacy for walking= 0-100% how confident are you that you can walk at a moderate pace for X amount of distance, Self –Efficacy Dyspnea = how confident are you 0 (not at all)-10 (confident) than you can control your breathing. State trait anxiety inventory (higher number= more anxiety), GDS= Geriatric Depression Scale (score of 5 > indicate possible depression, and 7> probable depression), CRQ= Chronic Respiratory Questionnaire (higher scores indicates =worse subjective experience), SF-36= 36 short form health survey (higher scores indicate = better HrQL**),** Fragmentation Index= number of sedentary bouts/ total sedentary time,

Table 9. Relationships Between Sedentary Time and Selected Variables (n=21)

Variable	Sedentary Time	P value
BMI	-.059	.799
FEV_1 post bronchodilator	-.447	.042
BODE Index	.450	.04
Comorbidities	-.162	.482
mMRC	.241	.293
GDS	.283	.214
Anxiety		
State	-.221	.335
Trait	-.267	.235
SF-36		
PCS	-.089	.702
MCS	.033	.886
CRQ		
Dyspnea	-.274	.230
Fatigue	.196	.395
Emotion	.060	.795
Mastery	.086	.711

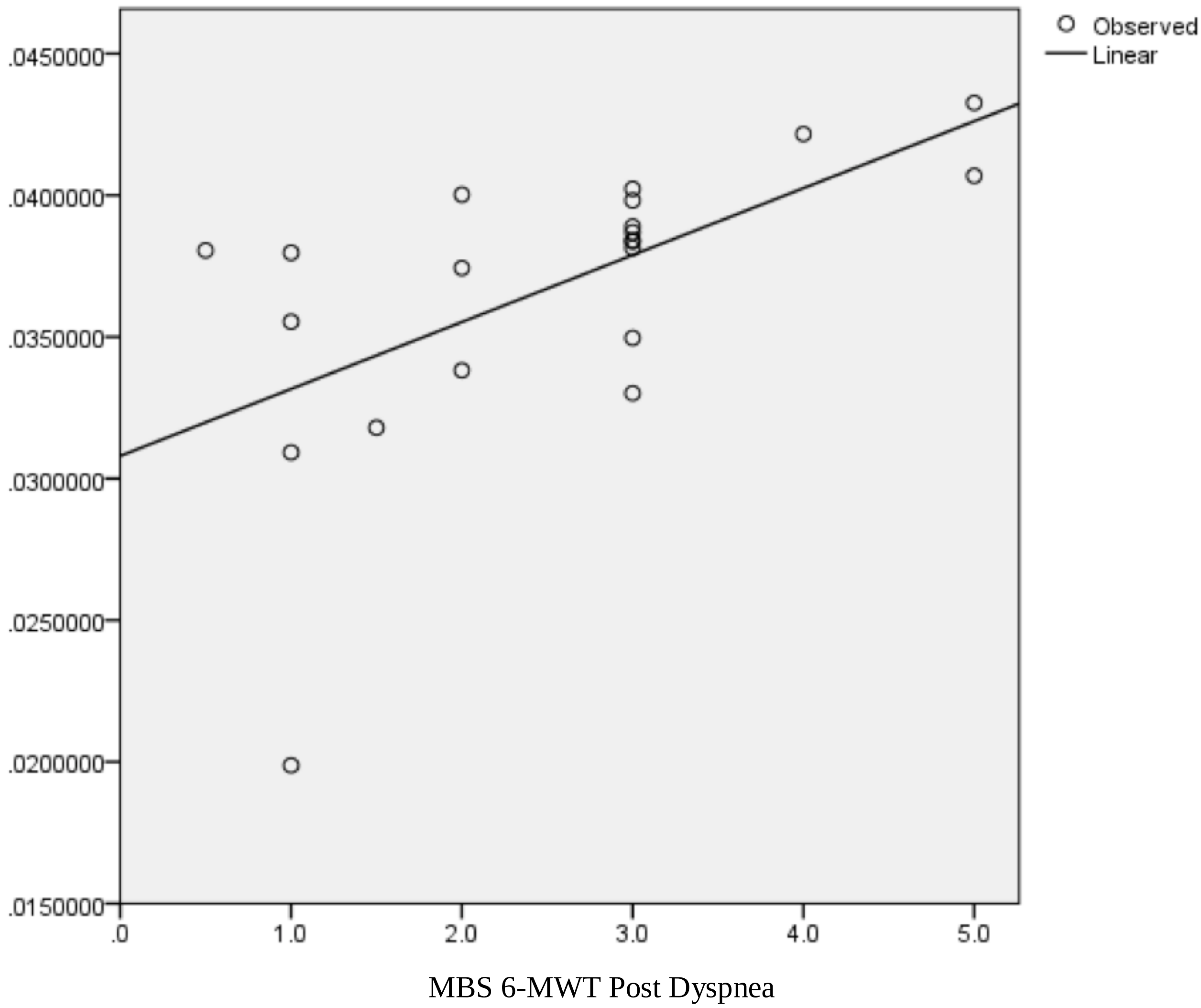
STAI= state trait anxiety inventory (higher number= more anxiety), GDS= Geriatric Depression Scale (score of 5 > indicate possible depression, and 7> probable depression), CRQ= Chronic Respiratory Questionnaire dyspnea domain (higher scores indicates =worse subjective experience of dyspnea in everyday life), SF-36= 36 short form health survey (higher scores indicate = better HrQL), Distance for walk conditions reported in meters (1 meter=3.28084 feet), Fragmentation Index= number of sedentary bouts/ total sedentary time, Step counts = average step count per hour. BODE = body-mass index (B), airflow obstruction as measured by the FEV_1 (O), dyspnea as measured by the mMRC (D), and exercise capacity (E) as measured by the six-minute walk distance (higher scores reflect decreased chance of survival within 4 years), mMRC= Modified medical Research council breathless scale (higher numbers indicate worse condition).

Table 10. Relationships Between Levels of Physical Activity, Fragmentation Index and Selected Variables

Variable	Sedentary Time	Light PA Time	Moderate PA Time	Fragmenta-tation Index
Age	0.4	-.03	.01	-.04
FEV1 % post broncho	.44*	.41	.31	-.08
Pack/years smoked	-.31	.31	.02	.30
BMI	-.06	.02	.38	-.03
Co-morbidity Score	-.16	.16	-.07	.17
6-minute walk				
Distance	-.170	.12	.45*	-.04
Dyspnea post-test	.28	-.28	.01	.59**
mMRC	.24	-.23	-.11	.39
BODE Index	.45*	.40	-.48*	.16
GDS	.29	-.28	-.05	.13
Self-Efficacy				
Walk 3 blocks	-.11	-.08	.19	-.22
Walk 2 miles	-.10	-.04	.51*	.00
Self –Efficacy Dyspnea	.09	-.10	.08	-.38
CRQ				
Dyspnea	-.27	.28	-.09	-.31
Fatigue	.19	-.17	-.05	-.30
Emotion	.06	-.04	-.12	-.17
Mastery	.08	-.08	-.02	-.06
SF36				
PCS	-.08	.09	-.09	-.39
MCS	.03	-.01	-.11	.34
Anxiety				
State	-.22	.18	.24	.08
Trait	-.27	.23	.25	-.03

*<.05, **<.01. Self Efficacy for walking= 0-100% how confident are you that you can walk at a moderate pace for X amount of distance, Self –Efficacy Dyspnea = how confident are you 0 (not at all)-10 (confident) than you can control your breathing, mMRC= Modified medical Research council breathless scale (higher numbers indicate worse condition), STAI= state trait anxiety inventory (higher number= more anxiety), GDS= Geriatric Depression Scale (score of 5 > indicate possible depression, and 7> probable depression), CRQ= Chronic Respiratory Questionnaire dyspnea domain (higher scores indicates =worse subjective experience of dyspnea in everyday life), SF-36= 36 short form health survey (higher scores indicate = better HrQL), Dyspnea post- test = dyspnea level rated by BORG after 6-MWT). PA = physical activity, Sedentary Time = average minutes in an hour, Light PA Time = average number of min in an hour, Moderate PA time = average number of min in an hour, Fragmentation Index= number of sedentary bouts/ total sedentary time.

Figure 1. Relationship Between Fragmentation Index and Post-Dyspnea Scores on the 6-MWD



MBS= Modified Borg Scale for dyspnea, Fragmentation Index = Sedentary bouts / total sedentary time

Determination Notice
Research Activity Does Not Involve "Human Subjects"

December 19, 2017

Alison Hernandez, PhD
Biobehavioral Health Science
300 North State St apt 5318
Phone: (305) 467-7847

RE: Research Protocol # 2017-1295
"Effects of Rhythmic Auditory Stimulation on Distance Walked Dyspnea in Individuals with COPD During 6-Minute Walk Test"

Sponsor(s): None

Dear Dr. Hernandez:

The UIC Office for the Protection of Research Subjects received your "Determination of Whether an Activity Represents Human Subjects Research" application, and has determined that this activity **DOES NOT meet the definition of human subject research** as defined by 45 CFR 46.102(f)/ 21 CFR 50.3(g) and 21 CFR 56.102(e)/ 38 CFR 16.102(f).

Specifically, this research will involve the secondary analysis of existing deidentified data only.

You may conduct your activity without further submission to the IRB.

Please be reminded of the need to address the need to enter into the Data Use Agreement through the UIC Office of Research Services.

If this activity is used in conjunction with any other research involving human subjects or if it is modified in any way, it must be re-reviewed by OPRS staff.

THE
UNIVERSITY OF
ILLINOIS
AT
CHICAGO

Data Use Agreement

This data use agreement (the "Agreement") is between **the Board of Trustees of the University of Illinois**, a body corporate and politic organized and existing under the laws of the State of Illinois, on behalf of the University of Illinois at Chicago ("RECIPIENT"), and **Edward Hines Jr., VA Hospital**, organized and existing under the laws of United States with its principal offices at Edward Hines Jr., VA Hospital, Hines, IL 60141 ("PROVIDER"). The parties may be referred to individually as "Party" and collectively as the "Parties".

WHEREAS, PROVIDER maintains certain information that RECIPIENT wishes to use for research, public health, or other purposes;

NOW, THEREFORE, the Parties, in consideration of the mutual promises and obligations set forth herein, the sufficiency of which is hereby acknowledged, and intending to be legally bound, agree as follows:

1. PROVIDER shall provide RECIPIENT with access to certain de-identified data that includes: (a) Data collected under an approved protocol titled *Rhythmic Auditory Stimulation to Enhance Exercise Capacity in COPD: A Pilot Study*, baseline data from the electronic database; and (b) any related know-how received by RECIPIENT from PROVIDER (collectively "Data") in accordance with the terms and conditions of this Agreement. A copy of the de-identified data will be made and transmitted to UIC using an encrypted VA thumbdrive. The file will be reviewed by the VA Privacy Officer prior to downloading the data to the UIC research drive.

2. The Data shall remain the sole and exclusive property of PROVIDER. PROVIDER shall be considered free, in its sole discretion, to distribute the Data to others for any purposes and to use it for its own purposes.

3. Alison Hernandez is authorized to use the Data or any part of it. Ms. Hernandez is a doctoral student in the College of Nursing. Eileen Collins PhD, RN is her dissertation chair.

4. RECIPIENT and each authorized individual agree as follows:

   a) Not to use or disclose the Data or any information contained therein other than as permitted by this Agreement or as required by applicable federal, state and local laws, rules and regulations, including the Health Insurance Portability and Accountability Act of 1996 (HIPAA) for the project/purpose *Rhythmic Auditory Stimulation to Enhance Exercise Capacity in COPD: A Pilot Study*;

   b) Not to distribute or release the Data to any person other than personnel under their direct supervision;

   c) To ensure that no one will be allowed to take or send the Data to any other location, unless written permission is first obtained from PROVIDER;

d) To use appropriate technical, administrative, and procedural safeguards to prevent use or disclosure of the Data other than as provided for by this Agreement;

e) To report to PROVIDER within (5) days any use or disclosure of the Data or any part of it not provided for by this Agreement of which RECIPIENT or any authorized individual becomes aware;

f) Acknowledge PROVIDER as the source of the Data in any publication arising from RECIPIENT's use of the Data

5. Recipient will not use the Data, alone or in combination with other information, to identify the individuals or contact the individuals or families from whom the Data was derived.

6. THE DATA IS TRANSFERRED TO RECIPIENT "AS IS." PROVIDER MAKES NO WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, AS TO THE DATA TRANSFERRED TO RECIPIENT AND PROVIDER SHALL NOT BE LIABLE FOR ANY DIRECT, INDIRECT CONSEQUENTIAL, SPECIAL OR OTHER DAMAGES SUFFERED BY RECIPIENT FROM ITS USE OR MISUSE OF THE DATA.

7. Except to the extent prohibited by law, the RECIPIENT assumes all liability for damages which may arise in RECIPIENT's use, storage or disposal of the Data. PROVIDER is not liable to the RECIPIENT for any loss, claim or demand made by the RECIPIENT or made against the RECIPIENT by any other party due to or arising from the use, storage or disposal of the Data by the RECIPIENT.

8. The PROVIDER may terminate this Agreement upon reasonable written notice to RECIPIENT. Upon termination for any reason, RECIPIENT shall immediately cease use of the Data, and destroy the Data, and any copies thereof, with written certification to PROVIDER of such destruction.

9. This Agreement shall be construed according to the laws of the state of Illinois, without regard to conflict of law provisions, and shall be deemed to have been executed in the state of Illinois.

IN WITNESS WHEREOF, the undersigned hereto have caused this Agreement to be executed by their respective authorized signatories.

THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS

Avijit Ghosh

By: Avijit Ghosh, Interim Comptroller

Date: 02/05/18

02/05/18

Signature of Comptroller Delegate Date

Michael D. Carr Interim Assoc. Dir. ORS

Printed Name and Title of Comptroller Delegate

PROVIDER

William A Wolf 507606 Digitally signed by William A Wolf 507606 Date: 2018.02.04 11:45:42 -06'00'

By: William Wolf PhD, Acting Associate Chief of Staff for Research

Date:

090110-00001, KW

Alison K. Hernandez, MS, RN
Curriculum Vitae
alisonkhernandez@gmail.com
305.467.7847

Education

2015-2018 PhD Nursing (Expected Graduation May 2018)
University of Illinois at Chicago, College of Nursing, Chicago IL

2014-2015 Bridges to the Doctorate (Non-Degree Program)
University of Illinois at Chicago, College of Nursing, Chicago IL

2012-2014 Master of Science
DePaul University, School of Nursing, Chicago IL

2008-2004 Bachelor of Arts in Psychology & Spanish
University of Miami, College of Arts and Sciences, Miami FL

Post Graduate Training

2015-2018 Future of Nursing Scholar, Robert Wood Johnson Foundation
University of Illinois at Chicago, College of Nursing, Chicago IL

2014-2015 Nurse Residency Program
Advocate Illinois Masonic Medical Center, Chicago, IL

Employment

2017- Present Adjunct Nursing Instructor
Nursing 332 Health Assessment
Nursing 301 Art & Science of Nursing
DePaul University, School of Nursing, Chicago IL

2017- Present Teaching Assistant
Nursing 531 Pharmacotherapeutics
University of Illinois at Chicago, College of Nursing, Chicago IL

2016-2017 Graduate Research Assistant
Music Enhanced Walking for Relief of Claudication Pain
(Internal Research Support Funding Program)
University of Illinois at Chicago, College of Nursing, Chicago IL

2014-Present Medical Surgical Trauma, Orthopedic and Neurovascular Surgery 'TONS' Unit, Nurse Clinician II
Advocate Illinois Masonic Medical Center, Chicago, IL

2015-Present Fitness Instructor at the University of Illinois at Chicago
Sports and Fitness Center, Chicago IL

2015-2016 Academic Tutor for the College of Nursing
University of Illinois at Chicago, College of Nursing, Chicago IL

2014 -2015 Health Educator for B.A.I.L.A. Research Project
University of Illinois at Chicago, Chicago IL

2008-2012 Clinical Research Coordinator, "John P. Hussman Institute for Human Genomics"
Miller School of Medicine, University of Miami, Miami FL

Service Activities

2016-2017 Albert Schweitzer Fellowship, Chicago Illinois, Peer Mentor

2016 Graduate Student Nursing Organization, University of Illinois at Chicago, Webmaster

2016 Health Professions Student Council, Univeristy of Illinois, Graduate Nursing Student Representative

2014 Sigma Theta Tau Committee, DePaul University, Research Chair

Honors & Awards

2017 National Association of Hispanic Nurses Scholarship

2017 Minority Trainee Development Scholarship (MTDS), American Thoracic Society

2017 Health Professions Student Council Travel Grant Award

2015 Robert Wood Johnson Future of Nursing Scholar Fellow

2013-2014 Albert Schweitzer Fellowship

2012 Robert Wood Johnson New Careers in Nursing Scholarship (NCIN)

Membership

2017-Present Member of the National Association Hispanic Nurses (NAHN)

2017- Present Member of the Midwestern Nursing Research Society (MNRS)

2017-Present Member of the American Thoracic Society (ATS)

2016- Present Member of the American College of Sports Medicine (ACSM)

2014- Present Sigma Theta Tau International Honor Society (STTI), Alpha Lambda Chapter

2008- Present Member of Sigma Delta Pi Hispanic Honor Society

Media

Hostettler, S. (2015, October 28). New program helps nurses move forward, faster, with PhDs. *UIC News*. Available at http://news.uic.edu/uic-selected-for-future-of-nursing-grant-names-two-scholars

Publications & Presentations

Hernandez K., A. 2017. Effects of Rhythmic Auditory Stimulation on Distance Walked and Dyspnea in Individuals with COPD During 6-Minute Walk Test**.** Student Poster Competition Winner. Midwest Nursing Research Society, Cleveland Ohio April 2018

Hernandez K., A. and Collins, E. 2016. In Severely Obese COPD Patients, Obesity May Contribute to Exercise Intolerance More Than Lung Function. Podium Presentation. American Thoracic Society, Washington, D.C. May 2017

Bronas U, Everett S, Briller J, Steffan A, Hannan MF, **Hernandez A**, Collins EG. Walking to the Beat to Enhance Walking Ability and Reduce Claudication: MUSICWALKER. Journal of Cardiovascular and Pulmonary Rehabilitation and Prevention (in press)

Professional License & Certifications

2018 Medical Surgical Nursing Board Certified (MSNCB)

2017 200-Hour Yoga Teacher Training Certification

2014 Registered Nurse, Professional License