Description of Project

Chronic obstructive pulmonary disease (COPD) is a pulmonary disease that causes dyspnea (i.e., breathlessness). Populations affected by this disease suffer from a litany of respiratory ailments including, shortness of breath and coughing due to overall degeneration of lung tissue and capacity\(^1\). Over 329 million worldwide are affected by COPD\(^1\)-\(^3\) and it is currently the third leading cause of death in the United States and the fourth worldwide\(^4\).

Patients with COPD have increased risk for cardiac events, osteoporosis, anxiety, and depression\(^1\). In addition, they suffer from muscle fatigue\(^7\), which is likely due to skeletal muscle changes, such as loss of mitochondria, fiber type shifting, and oxidative stress\(^14\). Decreases in physical activity are well documented in patients with COPD and are more than likely associated with these skeletal muscle changes\(^7, 9\). These skeletal muscle changes result in instability and/or a higher susceptibility to falls\(^6\). Previous research has sufficiently determined an association between falls and the presence of COPD\(^1, 2, 3, 10\).

Moreover, gait variability has been shown to be a useful predictor of future falls and diminished mobility\(^12\). Gait variability is defined as the stride-to-stride fluctuations while walking. Specifically, step width variability has been shown to be a predictor of past falls, future falls, and fear of falling in older adults\(^2, 5, 6, 9, 10\). Since patients with COPD walk with a more repetitive and more rigid step width pattern\(^12\), it is possible that their gait patterns could be associated with balance deficits as has been seen in older adults.

The overall aim of this project is to investigate whether step width variability is related to balance deficits in patients with COPD. My FUSE results from 2014-2015 show that there are balance deficits in patients with COPD as compared to healthy controls, which is also in line with current literature\(^1, 2, 4, 5, 11, 12, 15\). It is anticipated that patients who possess a more regular step width variability are also predisposed to more adverse scores on functional balance tests. Thus, creating an inverse relationship between the scores and a lesser degree of step width variability. This will ultimately tell us if a wider step width pattern significantly affects balance and may explain the higher incidence of falls within the COPD population\(^11, 15\).

This study will continue the results of my previous FUSE work by including data collected on these individuals. For the 2015-2016 FUSE, a correlation analysis will be made between gait (step width) variability and the most discriminatory functional tests that assess balance, as determined by my previous FUSE funded research. The most discriminatory tests are: Six Minute Walk Test (6MWT), the NeuroCom Balance Manager - Sensory Organization Test (SOT), the Timed up and Go (TUG) and the Fullerton Advanced Balance scale (FAB).

Activities, Process or Methodology

Data for ten patients with COPD and ten healthy controls will be used in this study. These subjects previously participated in my FUSE 2014-2015 funded study. All subjects were consented under the relevant IRB and screened using a self-reported medical history form to determine eligibility. Inclusion for patients with COPD was determined by a previous diagnosis and confirmed by spirometry (FEV\(_1/FVC < 0.7\))\(^12\). Patients with COPD were excluded if they used oxygen tanks or had comorbidities and/or prescriptions that may affect their musculoskeletal, neurological, pulmonary, or cardiovascular systems. All subjects (COPD / control) were excluded if they had any lower extremity injuries or surgeries within the last year.

Once eligibility was determined, subjects performed a series of balance tests as part of my FUSE 2014-2015 project. The 6MWT is an interpretable self-paced test that quantifies endurance through distance walked. Subjects were instructed to walk around a pre-measured track until they reached six minutes of total time walked, or stopped early due to fatigue. Once complete, their total distance walked was measured\(^1, 4\). The NeuroCom Balance Manager System is used for the sensory organization test, to assess the three sensory systems that control balance (vision, somatosensory, and vestibular) and provides an equilibrium score. There are six conditions (combinations of manipulating vision, proprioception and the vestibular system) and 3, 20 second trials for each. The resulting equilibrium score is ranked on a 0-100% scale, where 0% = reaching the point of falling or has fallen and 100% = no movement of the body while standing\(^8\). The TUG measures mobility and fall risks for time by having the individual rise from a chair walk out and back three meters, then sit back down. Times of less than 10 seconds are generally considered normal mobility\(^2, 4, 5\). The FAB is a series of balance tests to assess the subject’s ability to use their somatosensory cues to maintain upright balance in varying situations. There are ten
tasks in the FAB Scale and they are scored on a range from zero to four. Zero being unable to complete the task at hand and four being able to complete the task independently without assistance.

For this year’s FUSE project, the subjects enrolled in the balance study will return to for gait analysis for collection of step width variability. This secondary analysis will be submitted to the IRB. For the purposes of collecting data, subjects will wear a one-piece singlet and have 30 retro-reflective markers placed on anatomical landmarks. Data will be captured as they walk on a treadmill at their self-selected speed for approximately six minutes (120 Hz, Motion Analysis Corporation, Santa Rosa, CA). From these data, step width will be calculated over the six minute trial. Step width is defined as the distance from the most medial side of the left foot, to the most medial side of the right foot. The mean and standard deviation of the step widths over the trial will be calculated. The mean will indicate the central tendency, while the standard deviation will indicate the amount of variation. Quantification of the step width regularity will be provided by a calculation of sample entropy. Sample entropy is the probability that patterns in the step width will repeat themselves again. Sample entropy ranges from zero (a sine wave, perfectly repeatable) to infinity (white noise, random). A lower value for sample entropy indicates a more regular step width pattern and may explain the higher incidence of falls. To test my hypotheses, statistical correlations will be made between the step width data (mean, standard deviation, and entropy) and each of the balance test scores (6MWT, SOT, TUG, and FAB). The Pearson product-moment correlation coefficient will be used to measure the linear correlation between two variables. It is anticipated that once a line is fitted to the data, either a positive or negative correlation will be acquired. Moreover, answers to the following hypothesis are sought: are COPD patients with a more regular step width variability predisposed to more adverse scores on functional balance tests (measures) as compared to healthy controls? Are adverse balance test scores predictors of less step width variability in COPD populations versus controls? Is a wider step width in COPD populations of greater influence on the outcome of adverse balance test scores?

**Project Timeline**

- Fall 2015 (September – December) – Complete IRB modifications incorporating treadmill walking and analysis. (20+ hours)
- Spring 2016 (January – April) – Begin collecting gait data. Each subject will take 2 hours. (40+ hours)
- Summer 2016 (May – August) – Completion of data collections that could not be done in the spring. Perform comparative data analysis for all participants. Data analysis is estimated to take five hours per subject. (200 hours)
- Fall 2015 – Continue and finalize data and statistical analysis from all participants. Write abstract for 2017 Student Research and Creative Activity Fair and a national conference. (30+ hours)

**Student/Faculty Mentor Roles**

Preparation for this year’s FUSE truly began with the preliminary findings from last year’s FUSE and the potential to collect gait variability data. Once the potential for a comparative analysis was gleaned by myself, Dr. Yentes (faculty mentor) and her postdoctoral fellow, Dr. McCamley, guided my efforts in reviewing various collaborative articles. During my initial exploratory phase I began deducing the dependent variables. From there, the methodology formulated itself. After successful brainstorming and polishing my potential research questions, Dr. Yentes helped devise the overreaching aim to correlate the data. Finally, I began and effectively completed the application, having personally penned the draft and Dr. Yentes and Dr. McCamley reviewed it several times. Moving forward, I will be responsible for the IRB application and all data collection and analysis. Dr. Yentes will oversee the gait data collections and the many statistical analysis’ being performed. Through regular meetings, Dr. Yentes will guide my research process. Upon completion of all collections and analyses, an abstract and/or publication will be written by myself and reviewed and revised by my mentor.
Budget Justification

Of the $2,500 Fund for Undergraduate Scholarly Experience grant, a total of $400 will be used as stipends for research subject participation. Each of the 20 participants will receive $20 for their research participation, which will total $400. The remaining $100 will be used for supplies for the gait data collections. During a gait data collection, retro-reflective markers are used to identify anatomical landmarks. These markers are $75 for a set of 25 markers. In addition, the adhesive collar to attach the marker to the skin is $15 for a 100 collars. Plus shipping and handling, this is roughly $100 in supplies. As determined, any additional materials deemed necessary will be provided through the Biomechanics Research Building.

The remaining $2,000.00 will be used as a student stipend and will allow at least 20 hours a week to be committed to this project through the duration of the summer months of May-August. That will roughly equate to approximately $10.00/hr since more than 200 hours are anticipated being devoted to the project.
References
Dear FUSE Review Committee,

It is my pleasure to write a letter of recommendation for Mr. Jordan Freeman for a Fund for Undergraduate Scholarly Experiences grant. Jordan is currently an undergraduate student worker in the Biomechanics Research Building (BRB). As a faculty member of the BRB, I have been working directly with him since the Spring of 2014. I came to know Jordan as he was a student in my PE 2400 Anatomy & Physiology class in the Fall of 2013. He excelled in this tough course and I encouraged him to seek out a volunteer position within our laboratory. Jordan volunteered for several months within our laboratory, devoting any extra time he could. He proved to be a quick learner, eager to be involved and detail oriented. Hence, we hired him as a student worker starting in the Summer of 2014.

Since joining us, Jordan has worked on several multidisciplinary research projects however, he mainly works with me on my research projects focused on chronic obstructive pulmonary disease (COPD). In the past, his salary was covered by NASA EPSCoR mini-grant in which I was the PI. His salary is currently covered by another grant that I have investigating the use of a device to predict exacerbations in COPD. Over the past two years, Jordan has done an exceptional job in learning how to use high-tech, three-dimensional motion capture equipment, data processing, and any other tasks he has been assigned to complete. He has demonstrated that he is tremendously detail oriented and trustworthy in collecting and processing data. In addition to assisting with my grants, he has been performing research of his own.

Last year, Jordan submitted and was awarded a FUSE grant to investigate the relationship between age, COPD diagnosis, and balance deficits in a cohort of 40 individuals. Over the summer and this fall, he has successfully collected and analyzed his own data. He has completed data collections on all healthy controls and about half of the patients with COPD. He fully intends on submitting his findings to the UNO Research and Creative Activity Fair and at least one national conference this year. Jordan has even expressed interest in writing a manuscript based on his data. Truly, these are exceptional experiences for an undergraduate.

Recently, Jordan approached me about continuing his research experience. He wanted to extend his findings in balance further and see if they correlated with gait. He will use the same cohort from his 2015 FUSE grant and invite them back for gait analysis. After reading several articles, discussing these articles with a postdoctoral fellow working on my research team and myself, Jordan decided on the current research topic and aims. Jordan thought critically about the literature and was able to conceptualize the work being proposed in these aims. I have only provided feedback on his aims and drafts of his application. This project fits under my current research agenda focused on functional outcomes in patients with COPD. It is distinctly different from my current funding, which is focused on early diagnosis of exacerbations in COPD. Thus, this project is related, yet does not overlap with my funded research aims.

This is absolutely exceptional for an undergraduate student to be so interested in research. In fact, during the process of sending me versions of his application and me sending him feedback, he sent me an email that stated, “Perhaps I’m weird; however, I’m enjoying this process.” I responded by telling him, I didn’t think it was weird at all and that I predict he will get his PhD one day. I truly believe this. Jordan has shown a keen interest in asking the question, “Why?”. He is a critical thinker that is inquisitive, meticulous, and above all else, has high ethical standards. All key ingredients for a successful academician. I am truly excited to see where Jordan’s future takes him.

In addition to all of these things, Jordan is a Veteran of the United States Air Force. He has high moral standards and is so pleasant and polite. Every interaction with him is an absolute delight. He is respected by all members of the laboratory and even though he is an undergraduate, revered as a graduate student. I believe that this FUSE experience would be leveraged into research that is clinically relevant and will be presented at the UNO Research Fair and a national meeting. In addition, the experience gained from such an independent research project would be tremendously useful for a student that possesses the qualities that we as academics search for in all students, and find in a select few. It is with highest recommendation that I ask you to consider Jordan’s application.

Sincerely,

Jennifer M. Yentes, PhD