CONTROLLED PHONATION AND VOCAL REST PROGRAMS AFTER ACUTE VOCAL EXERTION IN HEALTHY ADULTS

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APPLICATION NARRATIVE FORM
Purdue University, Institutional Review Board

A. PROPOSED RESEARCH RATIONALE

Roughly 17.9 million adults in the United States are affected by voice disorders annually.[1] These disorders reduce quality of life and social interaction.[2] Voice disorders represent a significant financial burden, costing hundreds of millions of dollars in medical bills and resulting in an average of what is estimated to be as many as 39.2 work days per year.[3] Although the etiologies of voice disorders vary, speakers with voice problems consistently report vocal fatigue and increased effort to speak as the first symptoms. These speakers are often advised to cease voice use partially or completely, however, this may not be realistic given their occupation and the high cost to quality of life by not speaking.[4] The question then becomes, what should be done to mitigate the negative symptoms of voice problems when they occur, both to ease subsequent vocal function and to avoid eventual voice disorders.

In other anatomical subsystems, the idea of "cool down" following exertion is common. Data from multiple tissue types suggest that cool down following acute trauma may improve recovery. Emerging data suggest that a vocal cool down, may have a beneficial effect on vocal fold wound healing.[5] This work has primarily been done on animal models, however, preliminary data gathered in human subjects suggests that some individuals benefit from a cool down following vocally tiring events.[6] However, this question has not been systematically studied investigated in a rigorous manner that also enables us to understand the underlying mechanisms of this beneficial effect.

The proposed study will examine the effects of vocal cool down following exertion on voice measures and respiratory kinematics. Each speaker will also participate in a vocal rest experiment so we can compare cool down with vocal rest. Specifically, we seek to determine if a vocal cool down can mitigate the negative effects of a vocally tiring task as compared to vocal rest. We will assess voice measures and respiratory kinematics repeatedly to identify underlying mechanisms.

The study design will be a within-participant, repeated measures design. Once subjects are screened (see below), they will be scheduled to participate on two consecutive days. The procedures will be similar on both day. In brief, voice and respiratory measures will be collected on each day. Subjects will then perform a vocal exertion task and voice and respiratory measures will be collected again. The subjects will perform a cool down or vocal rest. Voice and respiratory measures will be collected again, followed by a second vocal exertion task and re-collection of voice and respiratory measures.

Because this study meets the NIH definition of a clinical trial, this study will be registered on ClinicalTrials.gov. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law, once the IRB is approved.

B. SPECIFIC PROCEDURES TO BE FOLLOWED

The proposed methodologies are routinely used in our laboratories. All proposed methodologies have been previously approved by the Purdue IRB. In addition, all devices utilized in this study are commercially available and will be used in accordance with their approved label.

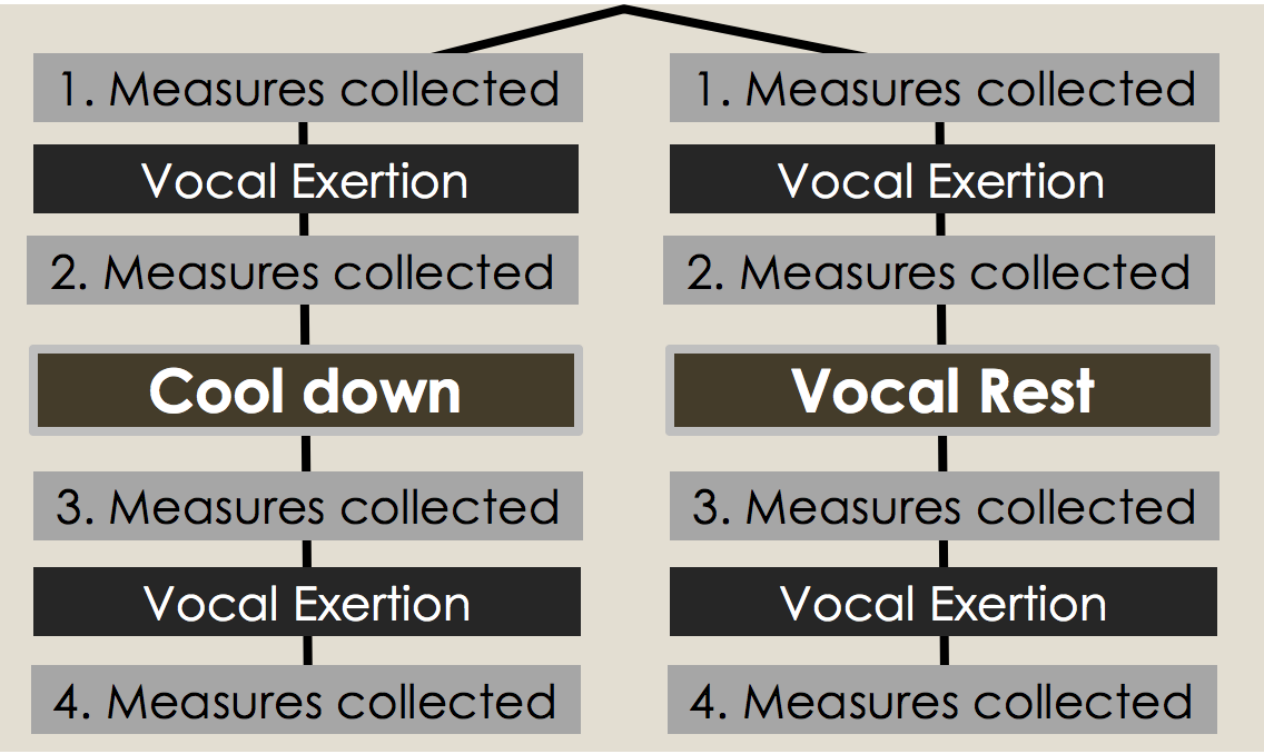
Protocol and Research Design:

Phone Screening and scheduling: verbal consent will be obtained before any questions will be asked over the phone. Once consent is obtained, screening questions will be asked (Document A). If subjects meet exclusion

criteria they will not be scheduled. If subjects are willing and able to participate, they will be asked to come back to the lab on two consecutive days at roughly the same time of day and will be scheduled.

Day 1: Informed consent will be obtained. Next, participants will complete a questionnaire (Document B) asking about current health status, medical history, medications, and occupational voice use. Then, participants will complete the Vocal Fatigue Index (Document C), the Vocal Handicap Index (VHI) (Document D) and the Reflux Symptom Index (RSI, Document E). Overall, these data will provide us a complete understanding of each participant's medical history, voice use, perception of voice and occupational voice needs. Then subjects will be scheduled for the following procedures if they are willing and available. Partial payment will not be provided if they are unwilling or unable to participate in the following procedures.

A schematic of the research design is shown below:



Measures: On each day the following procedures will be performed. All procedures – videostroboscopy, spirometry and all voice and respiratory measures will be carried out by the investigators listed on the personnel section (Sivasankar, PI; Fujiki, PhD candidate; Venkatraman, PhD student). Each investigator has at least a master's degree in Speech Language Pathology (the degree required to practice clinically) and has experience placing scopes in medical settings.

Spirometry will be performed using a Discovery Spirometer (Discovery Spirometer, Futuremed America, Inc..Granada Hills, CA) (See pamphlet in Document H). Spirometry is routinely carried out in lab and clinical settings and does not pose a risk to participants. A plastic filter attached to a cardboard tube will be placed in the participant's mouth. A tight seal will be maintained with the participant's lips and a nose clip will be used to occlude the nose. New filters, tubes, and nose clips will be used for each participant. The participant will be asked to complete breathing maneuvers like inhaling for as long as possible and either exhaling for as long as possible or exhaling fast and hard. There will be no discomfort caused to the participant during spirometry.

Videostroboscopy (9400 KayPENTAX videostrobe, Lincoln Park, NJ) (See pamphlet in Document I) with rigid endoscopes is completed by voice researchers and speech-language pathologists in routine clinical practice. Our lab has received IRB approval in the past to use this procedure. The PI (Sivasankar) has over 18 years of experience completing videostroboscopy with rigid endoscopes in two locations: Northwestern University and Purdue University. She has trained the co-investigators. Both are competent in this procedure and have been approved to complete this procedure in prior IRBs.

In preparation for each participant, the rigid endoscope will be wet disinfected with Cidex OPA (0.55% ortho-phthalaldehyde*)* and rinsed in water. A microphone will be placed externally on the participant's neck and secured comfortably with a Velcro strap. The participant's tongue will be draped with sterile gauze and held by the investigator who will be washed and gloved. The endoscope will be inserted through the mouth. The participant will be asked to produce an /ee/ sound with the endoscope in place. Some participants with a hyperactive gag may feel uncomfortable with the endoscope in place. The chance of eliciting a gag reflex will be minimized by changing the position of the endoscope. The endoscope will be placed in the participant's mouth for no more than 3 minutes. The participant will be able to breathe comfortably through their nose during the whole time. The scope may be placed up to four times per session. There are no particular risks associated with having the scope placed orally multiple times in a single day. Some subjects may experience increased gag reflex, but this is temporary and will not last after the scope is removed. Any participant who experiences discomfort or anxiety may withdraw from the study.

Voice measures will be obtained. Participants will wear a headset microphone. Participants will be asked to glide up and down their pitch range, produce different sounds at different loudness and pitch levels and sing some common songs. We will also collect the air pressure used for speaking and singing. The participant will be seated comfortably and a clean face mask with approximately a 2" length of plastic tubing will be placed around participant's mouth and nose. Participant's nostrils may be occluded. The airflow mask is vented with large screen covered holes so that it does not interfere with breathing or speaking. Each participant will receive a new disposable plastic tube. Participants will produce different sounds at different loudness and pitch levels with the mask in place. Finally, participants will use visual analog scales to rate how they feel about their voice.

Respiratory kinematic data will also be collected. To collect these data, respiratory bands will be placed around the subject's rib cage and abdomen. These bands will be attached with tape over clothing and do not pose any risk to the participant. Participants will be seated and asked to remain relatively still throughout these procedures. Next calibration will be completed. In order to achieve calibration, each participant will be asked to perform the following tasks while the movements of the chest wall and abdomen are recorded; quiet breathing, breathing while thinking a sentence silently, breathing in and out as much as possible, pulling the stomach in and pushing the stomach out a much as possible. The breathing tasks will be performed into a cardboard tube attached to a filter which is placed in the subject's mouth. These tubes are disposed of following each use and the filters disinfected. In addition, nose clips may be used during these tasks and are again disposed of after each use. Following calibration, subjects will be asked to read prepared sentences while wearing the respiratory bands.

In summary, spirometry will be collected one time per day, on both days. Videostroboscopy, voice measures and respiratory measures will be collected at 4 different times on each day. These times are (1) before the vocal exertion (see below; (2) after the vocal exertion (3) before vocal exertion (4) after vocal exertion.

Vocal Exertion Task: For this task, subjects will produce loud sounds for 15 minutes. Subjects will complete a vocal exertion task two times on each day.

Measures: Videostroboscopy, voice measures, and respiratory kinematics will be reobtained after the vocal exertion task.

Cool Down versus Vocal Rest: Participants will be counterbalanced to cool down or vocal rest such that each participant will complete both on different days. Each will take less than 15 minutes. For vocal rest, subjects will not speak. For cool down, subjects will complete voice exercises. These exercises are commonly utilized in clinical settings in order to help patients reduce throat tension and speak more efficiently. The exercises involve speaking and singing long vowels and pitch glides both with and without a straw. In addition, participants will hum and speak sentences with specific consonants (e.g. m and p). Each participant will be provided a new straw.

Measures: Videostroboscopy, voice measures, and respiratory kinematics will be obtained.

Vocal Exertion Task: Next, subjects will complete the second vocal exertion task for the same duration or shorter duration as the first task.

Measures: Videostroboscopy, voice measures, and respiratory kinematics will be obtained.

C. SUBJECTS TO BE INCLUDED

Participants will include males and females > 18 years with normal speech and language. Inclusion and exclusion criteria are listed below.

Exclusion criteria: Individuals will not be included in this study if they report cognitive impairments or disorders, craniofacial disorders (i.e., cleft palette or submucosal cleft), head and neck cancer, hearing difficulties, or have dentition problems or dentures which limit laryngeal imaging. Subjects will also be excluded if they report a gag reflex when they brush their teeth or refuse to undergo laryngeal imaging.

Inclusion criteria: Participants must be within the appropriate age range (18-65 years at the time of study) to participate in this study. They must score $\geq$80% for their age, weight, height and race on forced vital capacity and forced expiratory volume in 1.0 second on spirometry. In addition, the investigators must be able to obtain an image of the individual's larynx using rigid endoscopy to ensure that no gross laryngeal pathology is present. The presence of any pathology will preclude participation.

If any pathology is observed suggestive of an underlying condition, the subject will be referred back to their physician and will not be included in the study.

Participant availability and plan for dropout: We do not anticipate any difficulty in recruiting adults. We will recruit participants through fliers posted on campus and surrounding communities, ads in Purdue Today or similar newsletters, word of mouth, email, or phone. If participants drop out of the study before the end, they will be paid a partial payment and we will recruit a new participant to replace them.

D. RECRUITMENT OF SUBJECTS AND OBTAINING INFORMED CONSENT

Participants will be recruited by fliers throughout campus. All participants will be recruited by personnel who are trained in human subject protection. No undue pressure will be applied to individuals to participate. Subject information and data will be numerically coded and will not contain any identifying information. Informed consent will be obtained from all participants. All participants in this study will be adults (age 18 years and older) and will have the capacity to provide informed consent. Participants will be asked to participate in the study because they are healthy and have no overt laryngeal pathology.

During the initial phone call to potential participants who contact us via posted flyers, the participants will be asked to confirm that they are over 18 years of age and asked if they have any currently diagnosed voice disorders. They will be asked additional questions listed on (Document A). Participants will be informed that their voice and breathing will be examined in the study. Participants will be told about the duration of the study, and a brief summary about what they can expect, and scheduled for 2 consecutive days.

On the first day of the study, study personnel will utilize the initial 10 minutes to describe the study, answer questions for potential participants, discuss informed consent, and ask the participant to sign the consent form. Participants will then sign the consent form. They will be reminded that they are free to withdraw at any time. They will also be provided with information about the protocol for the study, the questionnaires, and recordings that are to be obtained. Additional time will be spent to clarify the procedure or answer any questions, if needed. All participants will be fully informed about the procedures. Participants will be shown the equipment and will have multiple opportunities to have all of their questions answered throughout the study.

E. PROCEDURES FOR PAYMENT OF SUBJECTS

Subjects will be compensated $25 for the first session and $35 for the second session. Partial payment ($5) will be provided to participants if they consent to the study and the measures but do not meet inclusion criteria or drop out of the study before completing a session. Participants will have the right to withdraw from the study at any time.

F. CONFIDENTIALITY

Participants in this research study will be identified by number and not by name so that their identities and personal information are kept confidential. Records of ongoing participation will be kept confidential in the laboratory in Lyles-Potter Hall. This laboratory is locked and only authorized lab personnel will have access to subject information. Subject identity and data will not be directly linked to preserve subject identity. Recordings will be stored on a password protected computer and backed to the laboratory server hosted by Purdue, which is password protected. Only authorized lab personnel will have access to the computer and drive. In addition, recordings will be completely de-identified. Recordings will not be destroyed at study closure. The results of the study may be published or presented at scientific meetings; however, participants will be identified in these reports by number and not by name.

G. POTENTIAL RISKS TO SUBJECTS

The investigators will explain and demonstrate the technologies and tasks to be used. There is always a risk of breach of confidentiality but the investigator will minimize this risk. There are no known risks in recording a person's voice production. Universal precautions (such as disinfecting the endoscope for 15 minutes prior to use and utilizing new tubing and disposable foam nose clips for each subject) will be employed. Endoscopy carries a minimal risk for the subject. Some participants may experience a temporary gag reflex which will subside after the endoscope is removed. Changes in head, tongue, and endoscope position will help minimize gag reflex. In addition, subjects may experience temporary fatigue following the vocal exertion task, but the effects will dissipate over time.

H. BENEFITS TO BE GAINED BY THE INDIVIDUAL AND/OR SOCIETY

There will be no direct benefit to the individuals participating in this study. However, this information will provide us with better understanding of how to minimize or prevent voice problems. With more research, we may be able to identify individuals at risk for voice problems

I. INVESTIGATOR'S EVALUATION OF THE RISK-BENEFIT RATIO

No major risks are anticipated from participation in this study. This study has the potential to demonstrate how prolonged speaking affects the voice. Because the risks of participation are minimal and the potential for gaining new information is excellent, the benefits of this study substantially outweigh the minimal risk of participation.

J. STATISTICAL ANALYSIS PLAN

Statistical analysis will be conducted using SAS (Version 9.4, 2013). Power analysis indicates an N of 30 subjects will be sufficient to answer study questions with reasonable statistical power. Dependent measures will be analyzed using linear mixed effect models. Fixed factors included in the statistical model will include time (baseline, post exertion task 1, post restorative strategy, post exertion task 2) and restoration strategy (controlled phonation or vocal rest). A time and restoration strategy interaction will also be included in the model. Participant will be included as a random factor in order to control for individual variation. Alpha level for significance will be set at $p < .05$. Tukey HSD tests will be used on post-hoc comparisons. In addition, Cohen's *d* for repeated measures will be calculated on significant post-hoc comparisons using the Cohen's *d* calculator for repeated measure designs developed by Psychometric.de (https://www.psychometrica.de/effect_size.html).

References

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