STUDY PROTOCOL
Respiratory Capacity and Swallowing Function in Spinal Disorders: A Pilot Study

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Introduction

This protocol covers a subproject formed from a larger project entitled *Physiological Flow of Liquids Used in Dysphagia Management*. The larger project has been reviewed and funded by the National Institutes of Health as a 5-year R01 grant awarded to the PI (Catriona Steele, Ph.D).

The overall goal of the project is to collect measurements of liquid flow through the oropharynx (i.e., mouth and throat) during swallowing. The factors that are expected to influence liquid flow include the liquid consistency (i.e., thin, slightly-thick, mildly-thick, moderately-thick, extremely thick) and the forces applied during swallowing (i.e., tongue pressures and swallowing muscle contraction). The objective is to determine how these factors interact to influence the flow of a liquid through the oropharynx. The focus of this project is to evaluate the flow of liquids of varying consistency in the spinal disorder population.

Data collection will take place at the Swallowing Rehabilitation Research Lab of the Toronto Rehabilitation Institute. Videofluoroscopy x-rays will be conducted on a purchased service basis in the diagnostic imaging department at the Toronto General Hospital. Data will also be collected via patient-report questionnaires.

Purpose and Specific Aims

Spinal disorders are considered a wide class of diseases and/or injuries that challenge the stability and function of the spinal vertebrae, spinal column, and associated structures. Spinal disorders can affect any level of the spine, resulting in a variety of sensory and motor impairments. In approximately 10-15% of cases, spinal disorders have a known pathology, such as a congenital condition, traumatic injury, or tumor (Boos & Aebi, 2008). Structural or nerve damage related to the spinal disorder may contribute to an individual's swallowing impairment. Three nerves with key functions in swallowing have been identified as susceptible to damage as a result of a spinal disorder: the hypoglossal nerve, the superior laryngeal nerve, and the recurrent laryngeal nerve. Damage to these nerves can affect swallowing safety and efficiency at the oral and pharyngeal phases, decreasing airway protection and increasing the risk of aspiration. In addition, injury or progressing disease at cervical and thoracic spinal levels can also impact an individual's respiratory capacity (Mansel & Norman, 1990). As respiration and swallowing are tightly synchronized, dysfunction in one process may greatly impair performance in the other. In this study, we propose to further examine the relationship between respiration and swallowing in the spinal disorders population, in order to better understand how impairment in one system may influence the other.

We have two specific aims:

Aim 1: To assess swallowing safety and efficiency for different consistencies in spinal disorders.

In this project, we will collect videofluoroscopic measures of swallowing in individuals with spinal disorders using barium stimuli across the continuum of liquid consistency. Static measures of tongue pressure generation during maximum isometric and saliva swallowing tasks

will be collected to provide reference data regarding tongue strength. Significance: This will show the impact of consistency on bolus flow through the oropharynx, controlling for the tongue forces used in swallowing. Thickened liquids are often used as a compensatory strategy for individuals with swallowing safety and efficiency concerns. Evaluating the flow of different liquid consistencies in the spinal disorders population may yield useful information regarding future therapeutic use of diet texture modification for individuals with swallowing impairments.

Aim 2: To explore the relationship between respiratory capacity and swallowing function in spinal disorders. In this experiment, we will collect reference data regarding respiratory capacity and concurrent measures of airflow pattern during swallowing with stimuli of varying liquid consistencies (measured under videofluoroscopy). Significance: This will determine how respiratory capacity may influence swallowing function, and specifically which swallowing parameters may be affected by reduced respiratory capacity, further explaining the relationship between respiration and swallowing in this population. The impact of fluid consistency will be incorporated into this analysis of respiratory-swallow relationships.

Methods

Participants

This project will aim to recruit a sample of adults, aged 18 years or older, diagnosed with a spinal disorder with an injury level at the cervical or upper thoracic level (thoracic segment 6 or higher). Participants will be asked to complete all data collection sessions: 1) intake appointment, 2) session 2 (videofluoroscopy).

Exclusion Criteria

Participants with spinal disorders will be accepted and deemed eligible for participation in the study provided they do not fulfill any of the following exclusion criteria:

- Prior history of swallowing, motor speech, gastro-esophageal difficulties, chronic sinusitis or taste disturbance.
- Neurological difficulties unrelated to their spinal disorder (e.g. Stroke, Parkinson disease, etc).
- Cognitive communication difficulties that may hinder ability to participate.
- Current use of mechanical ventilation
- External instrumentation around the head/neck that would obstruct the field of view during the videofluoroscopy exam (e.g. cervical collar).
- Type 1 Diabetes (due to the requirement to swallow stimuli containing starch based thickeners, which carry a significant carbohydrate load).
- Known allergies to latex, food coloring or dental glue (due to the probability that these items will come into contact with the oral mucosa during data collection).
- Children and pregnant women (due to the use of radiation during the videofluoroscopic examination).

- Occupational radiation exposure such that the addition of a videofluoroscopy is likely to yield a total exposure exceeding 10 mSv (i.e., half the allowed Ontario annual limit for occupationally exposed workers).

These exclusion criteria will be confirmed using a self-report questionnaire form at the time of intake into the study. Any questions will be clarified through discussion with the research assistant responsible for participant intake, and, where necessary with the principal investigator.

Recruitment

We propose to recruit approximately 30 participants with a variety of spinal disorders. Participants will be recruited from Toronto Rehabilitation Institute – Lyndhurst Centre using the Centralized Recruitment process. The Patient Research Liaison will pre-screen patients for eligibility in the study, and provide them with an information sheet discussing the aims of the study. If the individual is interested in participating in this study, the Patient Research Liaison will contact a member of the research team to organize further screening. Informed consent will be conducted by a member of the research team. The estimated cost of using Centralized Recruitment for this project is approximately $ 2307.95.

Stimuli

An array of barium stimuli in thin, slightly-thick, mildly-thick, moderately-thick and extremely-thick consistencies, defined using the International Dysphagia Diet Standardisation Initiative (IDDSI) gravity-flow measures, have been developed in the Swallowing Rehabilitation Research Laboratory for the purpose of this study. The barium stimuli will be prepared using E-Z-Paque® barium in 20% w/v barium concentration[84] with starch and gum-based thickening agents (Nestlé Resource® ThickenUp® and ThickenUp Clear®).

All stimuli will be prepared in the Swallowing Rehabilitation Research Laboratory not longer than 3 hours prior to scheduled use, according to a strict standard operating procedure. Following preparation, stimuli will be refrigerated until needed. Barium stimuli will be transported to the radiology suite at Toronto General Hospital in a cooler, as per routine clinical procedures.

Data to be Collected from each Participant

The following types of data will be collected from the participants:

a) An intake questionnaire noting age, sex, ethnicity, height, weight, and race data and confirming eligibility based on the absence of reported exclusion criteria.
b) During the intake process, we will review a list of conditions that could alter the results of the research study and identify whether any of these conditions apply. This will include disclosing the use of any medications that the participant is are currently taking, in order to allow us to control for the possible influence of medication on oral sensory and motor function. Medications do not qualify as the basis for exclusion. However, it is important for us to collect information regarding the use of benzodiazepines and

neuroleptic medications that are known to have possible effects on swallowing, particularly with respect to causing xerostomia (dry mouth).

c) History of injury/disease (e.g. level of injury, surgical approach used), swallowing function, and respiratory capacity
d) Static measure of tongue pressure using the Iowa Oral Pressure Instrument, consisting of 3 repetitions of maximum anterior tongue pressures and 3 saliva swallows
e) Respiratory measures including full vital capacity and tidal volume
f) Nasal airflow measurements, collected using a nasal cannula coupled with the KayPENTAX Swallowing Signals Lab
g) Tracheal sounds and accelerometry collected using the Patch. Digitized sound and accelerometry data will be transferred from the internal memory card on the Patch to a computer for analysis.
h) A videofluoroscopy recording of swallowing collected at a pulse rate of 30 pulses per second and video capture at 30 frames per second.

Data Collection Procedures

Prior to videofluroscopic data collection during the second session, the participant will be seated in a chair for sensor attachment.

A small patch will be attached to the participant's neck using double sided adhesive and medical tape. The tracheal sounds and accelerometry signals will be captured on an internal memory card on the Patch itself. Digitized sound and accelerometer data will be transferred from the internal memory card to a computer for analysis. Tracheal sounds and accelerometry have been used to diagnose sleep apnea, which is characterized by apneas and hypopneas. Non-invasive breathing recordings have been used in previous studies (REB#09-051, REB#10-019, REB#10-037REB#12-0042-AE, REB#14-7954D) and the latest version hardware in REB#15-8967-DE. This device has been proven safe in other research studies conducted here at TRI.

Figure 1.The Patch placement (reference REB#15-8967-DE).

Spirometry measures will be collected, including full vital capacity and tidal volume using a handheld spirometer.

The nasal cannula flexible prongs will then be positioned within the participant's nares, curving downwards, with the tubing of the nasal cannula wrapped around and behind the ears. The tautness of the cannula will be adjusted to fit the participant comfortably.

The nasal cannula will be connected to the KayPENTAX Digital Swallow Workstation Swallowing Signals Lab equipment, which is located on a properly insulated cart with an uninterrupted power supply and isolation transformer. This equipment and procedure has been used in prior experiments in the PI's lab, with no history of adverse events.

Participants will be asked to swallow the barium stimuli previously developed in videofluoroscopy, with concurrent measurement of nasal airflow. Videofluoroscopy will be performed at maximum temporal resolution (30 pulses/second) and captured at 30 frames/second. Participants will be asked to swallow 3 boluses per stimuli type for a total of 18 bolus sips: 3 sips of thin barium; 3 sips per barium consistency prepared with a gum-based thickener (slightly, mildly, moderately, and extremely thick), and 3 sips of moderately thick barium prepared with a starch-based thickener. The stimuli will be presented in order of increasing consistency. Participants will be asked to take naturally sized sips of each stimulus from cups containing 40 ml. Cup weights will be measured before and after each sip on a digital balance so that sip volume and mass can be calculated.

Data Processing

The videofluoroscopy recordings will be spliced into single bolus clips and the audio channel will be muted to remove cues that might bias rating. Blinded videofluoroscopy rating will then be performed in duplicate by trained raters in the Steele Lab following established procedures. Discrepancies between raters will be flagged and resolved at consensus meetings, as required. These procedures will yield a large number of parameters for each swallow, as listed below:

a) Bolus transit time from ramus of mandible to vallecular pit (in ms);
b) Bolus dwell time in pharynx from ramus of mandible to laryngeal vestibule closure (in ms);
c) Pharyngeal bolus transit time from ramus of mandible to upper esophageal sphincter opening (in ms);
d) Bolus transit time from ramus of mandible to tail exiting the upper esophageal sphincter (in ms);
e) Laryngeal vestibule reaction time, from the onset of laryngeal elevation till full closure of the laryngeal vestibule is achieved (in ms);
f) Amount of residual left behind in the valleculae and pyriform sinuses after the initial swallow (measured using the Normalized Residue Ratio Scale;

g) Number of swallows for the bolus;

The airflow measurements collected via the nasal cannula will be rated in duplicate by trained raters in the Steele Lab. Discrepancies in ratings will be flagged and resolved at consensus meetings, as needed. The following airflow measurements will be collected and analyzed.

a) Respiratory phase pattern pre- and post-swallow;
b) Respiratory pause duration.

The following airflow measurements will be collected via the handheld spirometer. These measures will be recorded from the device by a research team member.

a) Full vital capacity
b) Tidal volume

Tracheal sounds and accelerometry will be collected using the Patch, providing data regarding flow rate and intensity.

Data Analysis

We will determine the extent to which parameters measured during ASPEKT rating (Analysis of Swallowing Physiology: Events, Kinematics, & Timing) differ between participants with spinal disorders and reference data from the Steele lab for healthy individuals (REB#15-9431-D). Data analyses will focus on evaluating whether the physiological parameters identified using ASPEKT, primarily laryngeal vestibule reaction time, explain differences in primary swallowing outcomes (Penetration-Aspiration score and pharyngeal residue) between groups. The primary respiratory outcome measures (respiratory phase pattern and pause duration) will be compared between participants with spinal disorders and data referenced from related studies evaluating these patterns in healthy adults (REB#15-9431-D). Using path analysis, the relationship between swallowing physiology and respiratory capacity may be illustrated, and the resulting effect on swallowing safety and efficiency in this population.

In addition, the relationship between stimulus consistency and the two primary outcomes (Penetration-Aspiration score and pharyngeal residue) will be analyzed to further our understanding of the impact of different liquid flow levels on swallowing function and physiology in the spinal disorders population.

Risks and Benefits

Risks

The following risks will be disclosed to all participants prior to obtaining their consent to participate:

a) It is possible that participants may dislike the taste or texture of some of the thickened liquid stimuli in the study. Participants will be reminded that they are free to discontinue participation at any time.
b) It is possible that participants may experience some fatigue during the data collection session. Participants will be reminded that they should disclose any fatigue or discomfort to the research team, and that they are free to discontinue any particular session or to withdraw from the study at any time.
c) Participants will receive exposure to radiation during the videofluoroscopy. Based on a previous videofluoroscopic study that we have conducted in healthy adults (Molfenter and Steele, 2013), this study is expected to involve 118+/-18 seconds of radiation exposure, with an associated dose estimate of <0.35 milliSieverts. Moro and Cazzani (2006) showed that this dose (0.35mSv) corresponds to a risk of 1 in 39,000 of developing a radiation-induced stochastic effect from a videofluoroscopy. We will use a warning bell to alert the data collection team to exposure time, and will terminate the protocol at the first opportunity following the bell.
d) Aspiration (entry of material into the airway) is a possible risk during the videofluoroscopic swallowing study that will be performed. This risk is always present for videofluorscopic swallowing studies, which are intended to document the presence and severity of swallowing abnormalities, including (but not limited to) aspiration. When aspiration is observed, standard procedures will be followed to encourage coughing and throat clearing to expel the aspirated material. After the 4th bolus involving an observation of aspiration, the protocol will be terminated immediately. Any participant who experiences aspiration will be counseled regarding aspiration prevention strategies and aspiration-risk following the videofluoroscopy.
e) Choking is an extremely unlikely event. However, in the event of choking, routine emergency procedures will be followed. All study personnel carry current CPR certification.
f) In the unlikely event that an incidental finding is noted on the videofluoroscopy (such as a diverticulum or a mass) the attending SRRL licensed speech-language pathologist will consult the on-call radiologist and generate a clinical report documenting the observation. These findings will be communicated with the participant as per usual clinical practice.

Benefits

There are no benefits anticipated for participants in this study.

Privacy and Confidentiality

Routine practices for ensuring the confidentiality and privacy of all participants will be followed in this study. All research personnel at the Toronto Rehabilitation Institute are required to sign a confidentiality agreement at the time of hire. Participants will be assigned a non-identifying alphanumeric study code, and the master key for this code will be retained separately by the Principal Investigator in a password-protected file on a secure, password-protected, encrypted research server. Daily back-up of this research server is performed centrally at the Toronto Rehabilitation Institute to protect against data loss. Hard copies of the participant consent

forms will be maintained in a binder, kept in a locked filing cabinet in the Swallowing Rehabilitation Research Lab.

All waveform and videofluoroscopic data will be stored electronically on the secure, password protected, encrypted research server. Any hard copy data will be transcribed into an electronic file (stored on the server), and the hard copy records will be stored in a locked filing cabinet in the Swallowing Rehabilitation Research Lab. Only the participant's alphanumeric study code number will appear on the data collection sheets and in the data collection files.

Access to participant information and experimental raw data will be restricted to the study personnel named in this application. All records will be destroyed after 10 years under the supervision of Dr. Steele.

Compensation

Data collection for each participant will involve 2 separate appointments: a) intake session; b) Session 2 (videofluoroscopy and respiratory measures). Each appointment is expected to last approximately 1 hour. The intake session will be completed at Toronto Rehabilitation Institute – Lyndhurst, whereas the second session will be conducted in the videofluoroscopy suite at the Toronto General Hospital. Transportation to and from the Toronto General Hospital, for the second session, will be provided for participants and accompanying attendants. An honorarium of $100 will be provided to each participant who participates in the study. This will be paid at the end of the final study visit.

Transportation

Transportation to and from the Toronto General Hospital, for the second session, will be provided for participants and accompanying attendants. Participants and accompanying registered nurse will be picked up from Toronto Rehabilitation Institute-Lyndhurst, will be dropped off at Toronto General Hospital, and then will be returned to Toronto Rehabilitation Institute-Lyndhurst following completion of the second session. This service, including pick-up times, will be arranged by the research team, and communicated to the participant and nursing manager.

Conflicts of Interest

Professor Steele, the principal investigator, is a member of the board of directors for the International Dysphagia Diet Standardisation Initiative (www.iddsi.org), a not-for-profit corporation, which developed the framework for the labelling, classification and testing of liquid thickness that will be used in this study. Professor Steele also holds current and prior research contracts with Bracco Canada and Nestlé Health Science, who are manufacturers of the barium products and thickening agents that will be used in this study. She has also served in an advisory capacity on expert panels for Nestlé Health Science. These relationships will be disclosed to participants in the study information sheet. All products for use in the study will be purchased. Neither Bracco Canada nor Nestlé Health Science will have any role as sponsors of this study. Dr. Steele will not receive any financial payment, either personally or to the lab,

related to the use of Nestlé or Bracco products in this study. Teresa Valenzano receives a stipend from the University of Toronto and a scholarship from the Toronto Rehabilitation Institute.

Informed Consent Process

All participants who show an interest in participating will be provided with detailed information about this study via the Participant Information Sheet and Consent Form at least one week prior to the scheduled intake appointment. Only after confirming they have understood all the information that is provided and after verifying they have no more questions, can they sign the consent form. A copy of the consent form will be provided to them. When the ability to comprehend the study is in question, we will also request assent from the patient's substitute decision maker prior to enrolling a patient in the study.
The consent form includes a specific section requesting consent to use of study-related images for future educational and teaching purposes.

Scholarly Review

The larger project of which this is a subproject has undergone scientific review by the MFSR Study Section of the National Institutes of Health (USA).

Additional Ethics Reviews

There are no additional ethics reviews planned for this project.

Contracts

There are no contracts required for this project. This project will be conducted exclusively at the Toronto Rehabilitation Institute.

Budgets

All costs for this study will be covered by the grant received from the National Institutes of Health.

References

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