Shirley Ryan AbilityLab

MENTORSHIP GRANT APPLICATION

Cortical activity during swallowing in acute post-stroke inpatients

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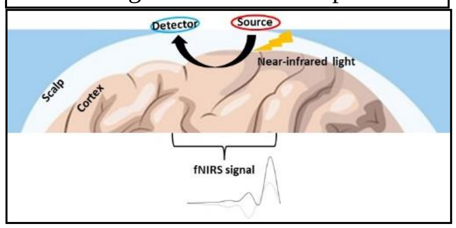
A. Introduction

Swallowing is a complex sensorimotor event involving precise and coordinated movement between respiratory and deglutition structures. Intact neural networks are critical for the fine integration between breathing and swallowing. Swallowing occurs during the expiratory phase of breathing[1]. This respiratory-swallow pattern (RSP) is essential for safe and efficient swallowing. Swallowing disorders (i.e., dysphagia) are present in at least 80% of stroke survivors[2,3]. Dysphagia increases length of hospital stay, increases cost of medical and hospital care, and negatively impacts mortality rate[4,5]. Moreover, dysphagia is associated with an increased risk of aspiration pneumonia, malnutrition, and dehydration[6-8]. Commonly, post-stroke dysphagia affects the respiratory-swallow coordination[9,10], increasing the risk of pulmonary infections.

Neuroimaging studies (e.g., functional magnetic resonance imaging - fMRI) have identified multiple cortical (e.g., primary somatosensory and motor cortices) and subcortical (e.g., thalamus and basal ganglia) regions involved in the swallowing process[11-13]. However, fMRI procedures do not allow for further investigation of cortical activity during swallowing in disordered populations because the image acquisition is highly sensitive to motion and individuals are required to lie in supine. Swallowing is an active process involving the movement of oral, pharyngeal, and laryngeal structures, which may produce artifacts during fMRI. Additionally, eating in a supine position increases the likelihood of aspiration (food entering the airway) in post-stroke patients.

Figure 1: Schematic representation of NIR light and cortical response



Functional near-infrared spectroscopy (fNIRS) is a noninvasive, portable, and low-cost brain imaging method that measures changes of oxygenated (O_2Hb) and deoxynageted (HHb) hemoglobin during cortical activity[14,15]. In this technique, light (near-infrared) is emitted by a probe (source) at the scalp and it can be absorbed by the blood flow or scattered by the tissue. Changes of light are then detected by another probe (detector) and displayed as a wave-like signal (Figure 1). Functional NIRS can be used while patients eat seated in a chair or at the bedside, allowing a more naturalistic environment to assess swallowing-related cortical activation. Additionally, fNIRS can be used during rehabilitation to monitor changes in brain activity during therapy. Previous studies have identified patterns of cortical activation during swallowing in *healthy adults*[16-18]. However, these studies have overlooked patterns of brain activity in individuals with dysphagia. Furthermore, no studies investigated changes in cortical activation following swallowing therapy and the relationship between abnormal RSP and cortical activity. Understanding the cortical mechanism underlying dysphagia and dysphagia recovery is critical to guide swallowing rehabilitation. This exploratory, clinical translational **study aims** to use fNIRS to investigate cortical responses during swallowing in a more naturalistic environment and determine whether swallowing therapy promotes brain changes in acute, post-stroke inpatients at Shirley Ryan AbilityLab (SRALab).

Aim 1: Investigate patterns of brain activity associated with normal and abnormal swallowing in post-stroke patients. Post-stroke patients with and without dysphagia will swallow varied liquid/food consistencies (e.g, juice, thicker juice, and pudding). We will (i) quantify the concentration levels of O_2Hb and HHb during swallowing in specific swallowing-related cortical areas, (ii) identify and compare regions that exhibit neural activation between post-stroke individuals with and without dysphagia, and (iii) compare RSP between post-stroke patients with and without dysphagia. We hypothesize that post-stroke patients with dysphagia will show decreased neural activation in swallowing-related areas compared to those without dysphagia. Moreover, atypical connectivity will be present in post-stroke individuals with dysphagia. Finally, patients with dysphagia will show abnormal RSP (e.g., swallow initiation during inhalation rather than exhalation).

Aim 2: Determine changes in cortical activation following swallowing therapy in post-stroke individuals with dysphagia. Post-stroke patients with dysphagia will receive their usual swallowing treatment (usual care) for 2 weeks by their speech-language pathologist (SLP). We will compare (i) O_2Hb and HHb concentration levels in swallowing-related cortical areas pre-and post-treatment and (ii) frequency of swallows initiated on exhalation pre-and post-therapy. We hypothesize that swallowing therapy will enhance cortical activity and the number of swallows initiated during exhalation.

B. Significance and Innovation

In 2022, SRALab admitted more than 500 stroke inpatients. Of these patients, almost 70% received a diagnosis of dysphagia and were treated by the SLPs at SRALab. Although many individuals with post-stroke dysphagia recover their swallowing function in the first few weeks, around 50% still have dysphagia after 6 months[19]. Persistent dysphagia is associated with long-term disability, institutionalization, poor quality of life, and increased risk of aspiration pneumonia[4,6,19]. Therefore, rehabilitation strategies that can drive cortical reorganization post-intervention may benefit post-stroke dysphagia recovery.

This proposed study is innovative because it will assess cortical activity during swallowing in a more naturalistic environment while acute post-stroke inpatients with and without dysphagia eat food with varied consistencies seated in a chair. Furthermore, this is the first study to use fNIRS to assess whether swallowing therapy enhances cortical activity post-intervention. Results of this study have the potential to advance the clinical understanding of the neural mechanisms of dysphagia and the neural recovery of swallowing, evidencing the potential neuroplastic cortical changes post-therapy. Moreover, it will have implications in post-stroke swallowing rehabilitation, guiding swallowing management to a neuro-recovery approach to care. These contributions will be translated to treating acute post-stroke dysphagia inpatients at SRALab, optimizing care planning and decision-making, and enhancing patients' outcomes and quality of life. Speech-language pathologists provide daily dysphagia treatment to acute stroke inpatients at their bedside or in the clinical labs. Clinicians can use fNIRS coupled with respiratory-swallow signals in treatment sessions due to their portability, low-cost, and easy set-up. Additionally, fNIRS is compatible with therapeutic devices, such as hearing aids and pacemakers, benefiting more patients.

C. Methods

Participants: We will include right-handed adults with a documented acute, unilateral hemispheric stroke without (Group 1; n=5) and with dysphagia (Group 2; n=5). Overall eligibility criteria include (i) Functional Oral Intake Scale (FOIS)[20] of 7 (Group 1) and 2 < FOIS < 6 (Group 2), and (ii) swallowing integrity or dysphagia diagnosed by a certified SLP with experience in swallowing diagnosis and management using the Mann Assessment of Swallowing Ability (MASA)[21] and confirmed via Modified Barium Swallowing Study (MBSS). Exclusion criteria include patients with a history of other neurologic disorders, major respiratory disorders, head and neck cancer, or other conditions that may impact swallowing function, and severe cognitive disorder that may prevent them from completing the study protocol.

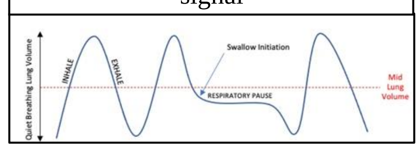
Procedures: An initial screening will determine preliminary eligibility criteria, including (i) a health questionnaire about medical history, stroke, and swallowing, (ii) FOIS, (iii) MASA, and (iv) auditory comprehension skills[22]. Subsequent evaluation with the MBSS will confirm final eligibility criteria.

Figure 2: Example of fNIRS montage

Treatment Procedures: Post-stroke participants with and without dysphagia will swallow varied liquid/food consistencies (e.g, juice, thicker juice, and pudding), while data will be acquired from (i) cortical activity using fNIRS (Figure 2) and (ii) respiratory-swallow signals: inhalation, exhalation, and breathing cessation during swallowing (Figure 3) using inductive plethysmography. The cortical regions of interest were identified in prior studies[16-18]. Post-stroke patients with dysphagia will receive swallowing treatment for 2 weeks (usual care) by their SLP at SRALab and complete the same protocol described in (i) and (ii) following dysphagia rehabilitation.

Outcome measures: ***Aim 1 – Patterns of brain activity:*** (i) quantification of O_2Hb and HHb during swallowing in the target cortical areas, (ii) identification of brain regions that exhibit cortical activity during swallowing, (iii) RSP. ***Aim 2 – Changes in cortical activity following therapy:*** (i) quantification of O_2Hb and HHb during swallowing in the target cortical areas pre- and post-swallowing therapy and (ii) RSP pre- and post-swallowing therapy.

Figure 3: Respiratory-swallowing signal



Anticipated Project Timeline

	0-3	3-6	6-9	9-12	12-18
IRB submission and approval	x	x			
Aim 1: Post-stroke participants without dysphagia		x	x		
Aim 1: Post-stroke participants with dysphagia			x	x	
Aim 2: Post-stroke with dysphagia			x	x	
Data analysis, statistical analysis				x	x
Dissemination of findings				x	x

Planned Deliverables

(i) Presentation for the Dysphagia Committee at SRALab during the monthly Dysphagia Team meeting; (ii) abstract submission for the Dysphagia Research Society Annual Meeting and the American Speech-Language-Hearing Association Convention; (iii) manuscript submission; (iv) grant submission (e.g., American Speech-Language Hearing Foundation, NIH early career R03).

D. Mentorship Goals

Training Goals: In this project, the mentees will receive mentorship from leaders in rehabilitation research in the areas of (i) fNIRS, (ii) translational research, and (iii) writing and professional presentations. Specific goals for each mentee are listed below.

<u>Mentee Clinical Investigator (Kristen Foran)</u>
Overall goals: The mentee clinical investigator will improve clinical research skills by conducting a research study in a clinical setting. Additionally, the mentee will learn new instrumentation (i.e., fNIRS and respiratory-swallow measures) for adjunct swallowing assessment and management that can be translated to patient care at SRALab. Finally, the mentee will develop translational research expertise and enhance communication skills for research purposes.
(i) Expand basic clinical research knowledge, including research procedures and design, eligibility criteria, recruitment of participants, consent form, data collection, and analysis, by helping to develop and conduct a clinical research project;
(ii) Advance translational research skills, including communication with patients about the research for recruitment, fNIRS technique for clinical use in dysphagia management, and collaboration with researchers on the gaps between clinical SLP and research in the field;
(iii) Enhance scientific communication skills by presenting the research findings for the Dysphagia Committee at SRALab.

<u>Mentee Investigator (Mariana Mendes Bahia)</u>
Overall goals: The mentee investigator will enhance her research competency by advancing her knowledge in neuroscience methods and instrumentations (i.e., fNIRS), and apply this learned skill to a clinical research study that can benefit swallowing rehabilitation, her area of expertise. Furthermore, the mentee will advance her translational research experience by working on a clinical research project. Lastly, the mentee will improve her scientific writing and oral presentation skills. This mentorship experience aligns with the mentee's learning, research, and career goals.
Specific goals:
(i) Advance technical knowledge in fNIRS, including data acquisition, pre-processing, and analysis, and apply this knowledge in an exploratory clinical research study in patients with dysphagia;
(ii) Enhance translational research skills, including collaborative work between researchers and clinicians, clinical population expertise with a focus on acute care, and practical training by completing a clinical research study;
(iii) Strengthen scientific communication and writing skills by presenting findings at professional conferences and writing a manuscript for a peer-reviewed journal;
(iv) Advance grantsmanship skills by learning how to communicate with a diverse audience, writing clear aims, research approach, and plan, and effectively communicate the potential impact of research in the field. In addition, the mentee will submit an external grant application.

Primary Mentor: Dr. Sameer Ashaie
Dr. Ashaie will facilitate this research project providing knowledge in <u>fNIRS</u> data acquisition, pre-processing, and analysis, <u>translational research</u> for acute care clinical population, and <u>grantmanship and scientific peer-reviewing</u> for future manuscript and grant submissions.

Secondary Mentor: Dr. Leora R. Cherney
Dr. Cherney will facilitate this research project providing knowledge in <u>translational research</u> for collaborative work between researchers and clinicians and acute care clinical population, and <u>communication, writing, and grantmanship peer-reviewing</u> for IRB submission, future presentations, manuscript and grant submissions.

Estimated Schedule for Mentorship: Mentees will meet weekly with primary mentor in the first and last three months of the project and at least monthly in the remaining months. Additionally, they will meet at least monthly with the secondary mentor.

E. References

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