Protocol

Pro00088290: How Related Are Speech Production and Reading? An Investigation of the Impact of Motor Tasks and Lidocaine on Reading Unfamiliar Words in Adults with and without Dyslexia.

NCT Number: NCT05854082

Date document created: October 23, 2019

Date document amended: June 25, 2024

Current version: 4.0

Author: Amberley V. Ostevik

Sponsor: Governors of the University of Alberta

Details

Pro00088290: How Related Are Speech Production and Reading? An Investigation of the Impact of Motor Tasks and Lidocaine on Reading Unfamiliar Words in Adults with Dyslexia.

Primary Investigator: Dr. Jacqueline Cummine

Location: Department of Communication Sciences and Disorders, University of Alberta, Edmonton, AB

Background

While there are no clinical trials that have explored the explicit connection between reading and speech production (as the current study is proposing) the print-to-speech model (Cummine et al., 2015) provides a framework for understanding how the recognition of visual word forms (i.e., reading) is built upon acquisition and production of speech. Knowledge of how a word sounds and feels when produced (i.e., auditory and somatosensory feedback, respectively) scaffolds the development of knowledge about what a word looks like (Hulme & Snowling, 2014). This notion that reading development is heavily dependent on oral language skills follows from many studies providing evidence that oral language skills (i.e., vocabulary, syntax) and phonological awareness skills are predictors of both typical and deficient reading ability (Catts et al., 1999; 2000; Vellutino et al., 1991; Wagner et al., 1997; Fletcher et al., 1994; Muter et al., 2004; Hulme & Snowling, 2014; Cheema & Cummine, 2017; Cullum, Fleming & Cummine, 2019; Pennington & Bishop, 2009, Catts et al., 2002; Tomblin et al., 2000; Hayiou-Thomas, 2010; 2017; Sices et al., 2007). Further, there are several nonclinical studies that provide convincing evidence that this connection needs to be better understood. For example, children with apraxia of speech, a motor speech disorder that results in an impaired ability to plan and/or program the sequential movements required for speech that is not attributable to deficits in motor physiology (e.g., weakness, or spasticity) or deficits in language (i.e., reduced comprehension; Duffy, 2013), are 1) at a high risk of developing a reading impairment and 2) have increased sensorimotor deficits. Newmeyer and colleagues (2009) evaluated the performance of 38 children with suspected apraxia of speech (CAS) on the Sensory Profile, a standardized assessment of sensory processing in children. Children with CAS had atypical sensory processing in five sensory factors, including oral sensory sensitivity. Increased oral sensory sensitivity in comparison to typically developing children has also been reported in children with specific language impairment (van der Linde et al., 2013), autism spectrum disorder (ASD; Kientz & Dunn, 1997) and attention deficit hyperactivity disorder (ADHD; Dunn & Bennett, 2002). In computational modeling, Terband and colleagues (2009; 2010) reported that the core impairment in CAS may be impaired feedforward commands secondary to reduced or degraded oral sensitivity, which fits well within the print-to-speech framework. Nijland et al. (2015) investigated oral form discrimination performance in children with CAS (i.e., identification of geometric shapes in the mouth) and reported that children with CAS scored significantly lower than typically developing children. Lower discrimination abilities are proposed to be an indicator of poor somatosensory function. In our own lab, we have found that oral form discrimination performance in adults is related to their reading performance (Cummine et al., in submission, 2020). Finally, Murray et al.

(2014) reported that sensory cueing approaches (which place emphasis on the relation between movements and auditory and somatosensory information via auditory, and touch, pressure, kinesthetic and proprioceptive cues) are the most effective for treatment of CAS. Such results suggest that sensory cueing approaches either target the underlying impairment directly (i.e. restorative) or compensate for deficits (i.e. compensatory). The identification of sensory difficulties in children with CAS is important to understand speech characteristics and treatment efficacy in this population. These findings warrant additional investigations to understand if and to what extent somatosensory processing contributes to speech production and reading deficiencies in healthy and impaired adult and pediatric populations.

We have also previously attempted to determine the influence of speech production feedback on reading performance by measuring reading performance in adults while adding an additional motor component (i.e., lollipop, bite bar, lidocaine). These somatosensory perturbations have the potential to alter and/or decrease the sensory feedback from the articulators in the mouth.

We found that the lollipop had a faciliatory effect (i.e., faster response times) in the orthographic lexical decision tasks but no effect on the phonological lexical decision tasks or picture categorization tasks. In contrast, the lidocaine had a faciliatory effect (i.e., faster response times) in the phonological lexical decision tasks, but no faciliatory effects on the orthographic lexical decision tasks or picture categorization. Finally, the bite bar did not impact performance in any of the three tasks. However, we do not know if these effects (i.e., lollipop, bite bar, lidocaine) hold for an adult population with reading disorders.

The investigational product we are requesting approval to use is Lidocaine Hydrochloride Oral Topical Solution 2% USP. This oral topical anesthetic will temporarily numb the participant's articulators. This clinical trial will be conducted in compliance with this described protocol, GCP and the applicable regulatory requirement(s).

Purpose | Objectives

1. To determine the effects of three different somatosensory perturbations (i.e., lollipop, bite bar, lidocaine) on reading performance (i.e., speed, accuracy) in adults with dyslexia.
2. To compare the findings with a previously completed study using a population of adults with typical (i.e., normal) reading abilities (Cummine et al., in press).
3. To better understand how the speech production system contributes to reading performance. The information will help refine the currently accepted speech and reading neural models.

Study Design | Trial Design

Participant | Subject Criteria

Inclusion criteria. Thirty adults (i.e., ≥ 18 years of age) of either sex or identified gender with diagnosed or self-reported dyslexia will be recruited to participate in a within subjects repeated measures design. Thirty participants (18+) without dyslexia will also be recruited as a control

group. All participants will need to be proficient in English as the assessment materials are only available in English.
Reading disorders are rarely formally diagnosed because of many factors including but not limited to: timing in educational system for assessments, comorbidities with higher priority disorders (i.e., apraxia of speech, ADHD, etc.) and cost. Self-reported reading challenges are more accurate at identifying potential participants. Self-reported reading disorders will be confirmed/verified prior to enrollment via standardized reading measures.

Exclusion criteria. Participants must have no personal or family history of adverse reactions to anesthetics to complete all the conditions. Participant who cannot consume sugary products will be excluded. Additional exclusion criteria include: severe kidney disease; severe liver disease; treatment with class I antiarrhythmic drugs (such as mexiletine) or class III antiarrhythmic drugs (such as amiodarone); lack of integrity of oral mucosa; allergy to non-medicinal ingredients and preservatives (and related compounds) of Lidocaine Viscous, such as methylparaben, propylparaben, paraaminobenzoic acid, saccharin, artificial colours and flavour; concomitant use of another anaesthetic containing lidocaine or another amide; participant being pregnant or suspecting that she might be pregnant; negative pregnancy test is required for women of childbearing potential.

Women of childbearing potential (WOCBP), i.e. assigned at birth females who experienced menarche and are not sterile or postmenopausal, may be included in the study, provided that they use an acceptable method of contraception, such as: hormonal contraceptives (e.g. combined oral contraceptives, patch, vaginal ring, injectables, and implants); intrauterine device (IUD) or intrauterine system (IUS); (partner's) vasectomy, tubal ligation; double barrier methods of contraception (e.g. male condom plus spermicide , cervical cap plus spermicide, diaphragm plus spermicide). Abstinence is acceptable provided that it is consistent with the participant's usual lifestyle.

Adult participants must weigh at least 50 kg or 110 lbs to avoid any possible toxic effects from the lidocaine.

Qualified Investigator (QI) Physician:
Dr. Caroline Jeffrey, MD
Suite 903
College Plaza
8215 112 Street NW
Edmonton, AB
Phone: 780.540.2111
Fax: 780.540.2114

Subjects that do not meet these criteria when contacting researchers will not be scheduled for collection. Participants will be immediately withdrawn (i.e., collection stopped) if they are unable to perform reading assessments, they report any adverse reaction or a desire to discontinue. If the participant withdraws or their participation discontinued, their data will be retained for analysis, unless the participant requests the data be destroyed. Any withdrawn participants will be replaced with additional recruitment. No follow-up is planned for withdrawn

participants unless they experience an adverse reaction that require medical follow-up and reporting.

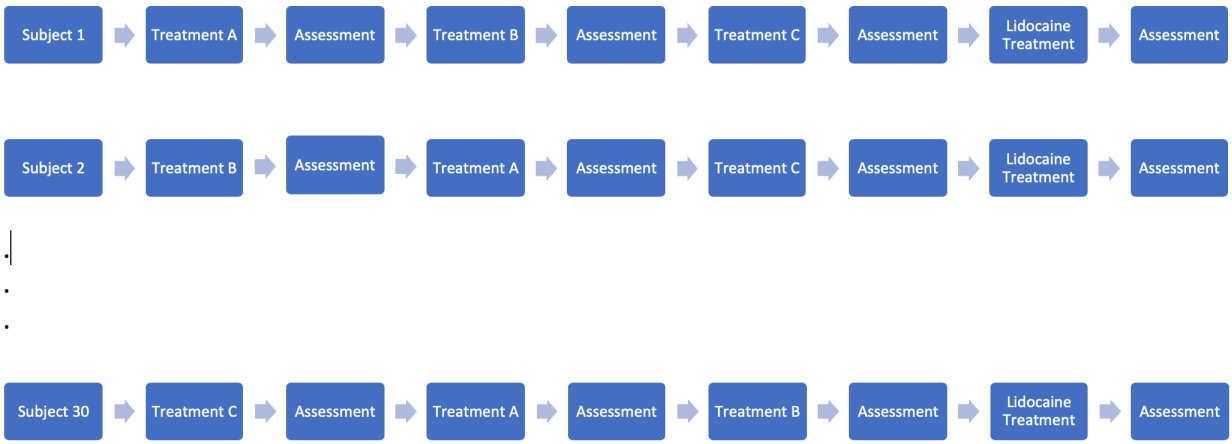

Figure 1. Schematic of repeated measures design

Methodology

The primary endpoint is reading response time and accuracy for each word type with and without oral perturbation.

The individual will be required to attend one collection session at the Clinical Sciences Building at the University of Alberta which will last no more than 90-minutes. Twenty percent (i.e., 12) of recruited participants will complete the the protocol below over two separate 60-minute sessions to investigate the effects of order, fatigue, etc.

During the session, participants will:

1. Read and complete an information and consent form (less than 10 minutes to complete).
2. Complete a pre-collection questionnaire to gather information such as age, sex and allergies (less than 5 minutes to complete).
3. Any participant reporting a personal or family history of adverse reactions to anesthetics will not be enrolled. If a participant reports any concerns or adverse reactions during the collection session, collection will immediately stop, and their participation discontinued.
4. If the participant is enrolled, they will be assigned a randomly generated identification number. All of their files and documents will be labelled with this number.
5. Each participant will also be randomly assigned to one of six possible task orders. Neither participants nor experimenters will be blinded to these conditions. This is documented in a hard-copy log.
6. Participants will be fit with an fNIRS cap to measure brain signals.
7. Then complete three computer generated tasks under four conditions (a, b and c will be randomized):
    a. No sensory perturbation
    b. Lollipop
    c. Bite bar
    d. Lidocaine – this condition will always be completed last.

8. The comparators to the lidocaine are no sensory perturbation, a candy lollipop and candy bite bar. All candy is obtained from the grocery store and are individually packaged. The lidocaine will be dispensed by a pharmacist and administered by the research team.
9. For the three computer generated tasks (randomly administered), accuracy and response time will be measured by the computer:
    a. Task 1 (orthographic lexical decision): involves deciding whether a series of letters formulates a word or a nonword. Individuals will press the 'g' key if it is a word and the 'h' key if it is a nonword. Stimuli are single, monosyllabic, 4-7 letter length, words and nonwords.
    b. Task 2 (phonological lexical decision): involves deciding whether a series of letters sounds out a word or a nonword. Individuals will press the 'g' key if it is a word and the 'h' key if it is a nonword. Stimuli are single, monosyllabic, 4-7 letter length, words and nonwords.
    c. Task 3 (picture categorization): requires participants to make a judgement about whether a visually presented object is an animal or not. They will press 'g' if the object is an animal, and 'h' if it is not an animal.
10. Complete a short questionnaire rating and describing the numbness caused by the lidocaine (less than 5 minutes to complete).

Treatment

Each participant will swish 15 mL (one tablespoon) of the Viscous Lidodan 2% in their mouth for 60 seconds, then spit into a sink. This amount is the recommended manufacturer dosage. This will occur once during the one collection session. Viscous Lidodan 2% (i.e., Lidocaine Hydrochloride Oral Topical Solution 2% USP) is a topical anesthetic. The numbing effects of Viscous Lidodan 2% should take effect after five minutes and last around 30 minutes.

No other topical oral anesthetics are permitted to have been administered in the day before the trial. No details are required on any other medications.

Safety Assessment

Safety Assessment/Monitoring and Risk Mitigation. Each participant completes a pre-collection questionnaire where it asks all subjects to report any personal or family history of adverse reactions to anesthetics. This is a hard-copy questionnaire that is completed by the participant after the informed consent form, but before collection begins. It is reviewed together with the experimenter and participant before collection commences. Participants will be informed prior to beginning the experiment that they may withdraw at any time. They will be monitored throughout the experiment by research staff for signs of distress or adverse reactions (e.g., redness, itching or swelling of skin, hives, burning, stinging, or any other skin problems, swelling of the neck area, or any difficulty with breathing). The QI will be available via phone/pager during administration of Lidocaine in case of adverse event(s) for assessment/triage/treatment/follow-up as clinically indicated.

If any reactions or adverse effects (i.e., redness, itching or swelling of skin, hives, burning, stinging, or any other skin problems, swelling of the neck area, or any difficulty with breathing)

are observed by the experimenters during collection, the QI will be called and the experimenter will escort the participant to the hospital emergency room connected to the Clinical Sciences Building. After the collection session is over, the participant will be instructed to report to their nearest emergency room if they experience any reactions or adverse effects. Participants will be informed that they should avoid eating and drinking and exposure to extreme hot or cold temperatures (e.g. food, drink) until complete sensation has returned. The numbness may also increase the risk of unintentional biting (e.g., cheek).

The lidocaine condition will always be lastly completed so its effects will not interfere with the other conditions. Each participant will be asked to complete a questionnaire after collection to localize and rank their numbness on a provided schematic. And adverse events reported by the participant will be recorded on this document and reported immediately to the qualified investigator. After the collection session is over, the participant will be instructed to report to their nearest emergency room if they experience any reactions or adverse effects. Topical anesthetics in the mouth may impair swallowing. The numbness may also increase the risk of unintentional biting (e.g., cheek). The qualified investigator, an otolaryngology head and neck surgeon, will follow-up with the subject as she deems appropriate. All serious unexpected adverse drug reactions (SUSARs) will be reported to Health Canada as mandated per C.05.014 (1) of the FDR.

Budget Considerations

Participants will be offered a small honorarium ($20.00) for taking part in the study.

Experiment Location

6-104, Clinical Sciences Building, University of Alberta.

Statistical Analysis

Given the between groups nature of the sensorimotor perturbation (i.e., lidocaine vs. no lidocaine groups), we will first run a 2 x 2 x 4 x 2 ANOVA with group (lidocaine vs. no lidocaine), task (spell vs. sound), word type (exception words, regular words, pseudohomophones, nonwords), and time (pre-lidocaine vs. post-lidocaine), as the factors of interest. If the 4-way interaction is significant, a series of mixed ANOVAs will be run to test the effect of sensorimotor perturbation for each of the reading tasks. The independent variables will be time (pre-perturbation vs. post-perturbation), word type (exception, regular, pseudohomophone, nonword) and group. An ANOVA was also be run to test the effect of the sensorimotor perturbation for the control picture categorization task, with the independent variables including time (pre-perturbation vs. post-perturbation) and group. The dependent variable will include response time and accuracy. Bonferroni corrected *t* -tests were used to explore significant effects of the lidocaine on task performance. No interim analyses are planned. The data will be analyzed when thirty subjects have participated.

Data | Documents

The data will be kept confidential and no personally identifying information will be linked to the data. All data will be reported in aggregated form. The data and consent forms will be stored securely at the University of Alberta by the principal investigator. The investigators and institution will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspections, providing direct access to source data and documents.

All data and documents relating to the clinical trial will be stored for a minimum of twenty-five years after completion of the study.