Study Protocol and Statistical Analysis Plan

Optimizing Soft Speech Recognition in Children with Hearing Loss (SoftSpeech)

Version 3

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Optimizing Soft Speech Recognition in Children with Hearing Loss

1 Background

Children with hearing loss have expressed preferences regarding how their hearing aids function in noise and when listening to low-level inputs in quiet environments (Scollie et al., 2010). In general, listening comfort is reduced in noise and listening clarity is reduced for low-level conversations or when listening at a distance from the talker. Although noise management features and remote microphones can help in such situations, management of the full landscape of listening environments is currently beyond the reach of these technologies. For example, neither feature provides auditory access to low-level input from multiple talkers at a distance, which is problematic given the importance of overhearing for vocabulary learning in young children.

A study by Jace Wolfe and colleagues (Wolfe et al., submitted) showed that, even when aided, children with hearing loss had significantly poorer speech recognition at 40, 50 and 60 dBA compared to children with normal hearing. Furthermore, they showed that increasing hearing aid gain for very low-level inputs produced a statistically significant improvement in syllable-final plural recognition and a non-significant trend toward better monosyllabic word recognition at very low presentation levels. Additional research is needed to document low-level speech recognition ability of children with hearing loss as well as the potential benefit or detriment of increasing hearing aid gain for low-level inputs.

A new feature in adult hearing aid technology known as “Speech Enhancer” has been shown improve low-level speech perception in adults with hearing loss; however, the effect of Speech Enhancer on speech recognition in children is not yet known.

2 Objectives

The primary objective of this study is to evaluate whether soft speech recognition in quiet is significantly improved with Speech Enhancer "on" at the default setting (moderate) compared to Speech Enhancer “off” in children with moderate (N3) to severe (N5) hearing loss.

Secondary objectives are to evaluate the potential interaction with comfort in children with moderate to severe hearing loss, and to demonstrate that hearing aids compensate for hearing loss in children.

3 Description of the investigational device

Copy from chapter 3.1 (Intended purpose of the investigational device in the proposed clinical investigation) of original CIP. The device name can be replaced by investigational device.

Hearing aids are non-surgical medical devices that enable people with impaired hearing to hear sounds again, which could not be heard previously due to a hearing loss.

The intended purpose of the hearing aid claims a compensation of the hearing impairment, which is a recognized disability category, and therefore the hearing aid is considered a medical device. The hearing aid is intended to amplify and transmit sound to the ear and thereby compensate for impaired hearing. Hearing aids are programmed to the individual hearing loss of an intended person and must therefore only be used by this intended person.

For this study, the intended patient population is children under 18 years of age with hearing loss ranging from moderate to severe.

The study will include the following types of hearing aids: Naída P-PR and Naída P-UP behind-the-ear (BTE) devices, and Audéo P-R receiver-in-the-ear (RIC) devices. Although BTEs and RICs are both worn behind the ear, their receiver locations differ. In BTE devices the receiver is located in the internal device housing whereas with RIC products the receiver is worn in the ear canal.

4 Design of the clinical investigation

This confirmatory clinical investigation will be executed at Hearts for Hearing. It is a single-group, single blind intervention study with each participant serving as his or her own control.
However, in certain conditions participant blinding is not feasible (i.e., aided versus unaided performance).
The outcome measures being assessed include: speech recognition in quiet with CNC words and comfort ratings using a Multiple Stimuli with Hidden Reference and Anchor (MUSHRA) procedure and looped sentences overlaid with low-level transient noise.
Four different hearing aid conditions will be assessed in this clinical investigation: unaided (no amplification), aided with SE "off", aided with SE "moderate" = 14, aided with SE "strong" = 20.

- **Unaided**: No treatment, (i.e., no Phonak hearing aids are worn). Unaided condition acts as control intervention for intended use. Blinding is not possible for this condition.
- **Aided with SE "off"**: Aided condition with SE turned "off". Provides control intervention for intended use and baseline for comparison to SE "on" for speech recognition in quiet and preference and comfort ratings.
- **Aided with SE "moderate":** Aided condition with SE turned "on" at the default moderate setting. Acts as the intervention being compared to SE "off" for recognition in quiet and preference and comfort ratings.
- **Aided with SE "strong:** Aided condition with SE turned "on" at the strong setting. Acts as the intervention being compared to SE "off" for speech recognition in quiet and preference and comfort ratings.

Hearing aid program order (speech enhancer settings) will be randomized for all testing conditions except for CNC at 50 dBA Quiet with SE Off and unaided CNC in 50 dBA Quiet. Those conditions are administered first to establish candidacy for further aided testing and obtain data for the intended use objective. A rand function in excel was utilized to create the randomized list of SE settings for all participants for the remaining conditions, which include a second administration of SE Off to minimize any changes associated with learning the task.
Program changes affecting SE strength (i.e., off, moderate, strong) will be initiated via the app by the researcher and will be unknown to the participant.
Study tasks will be completed in the following order, which reflects prioritization of testing related.

1) Aided CNC Words @ 50 dB HL SE Off
2) Unaided CNC Words at 50 dB HL
3) Aided CNC Words 40 and 50 dB HL
4) Aided subjective comfort ratings

5 Risks and benefits of the investigational device and clinical investigation

The risks associated with participating in this study are minimal; study procedures are within the scope of practice of the research audiologists and the incidence of adverse events associated with device use is low. Moreover, given the short duration nature of the study and exclusive use of hearing aids in the laboratory under supervision of qualified research personnel, risks associated with potential long-term product insertion, use and maintenance are substantially reduced.

6 Endpoints

The primary endpoint is percent correct score on the CNC word test. The rationale is that this clinical test has been used previously in research by Wolfe and colleagues who showed improved soft speech recognition with increased gain for low-level inputs.
The secondary endpoint is subjective report on a MUSHRA task. It has been used previously to assess self-perceived comfort and self-perceived benefit from new features such as Speech Enhancer and can give an indication as to whether certain settings (i.e., strengths) are preferred.

7 Inclusion and Exclusion Criteria

Subjects fulfilling all of the following inclusion criteria are eligible for the investigation:

- children 4 - 12 years old
- native English speakers with good spoken communication skills
- Healthy outer and middle ear
- capable of achieving aided speech intelligibility scores on open-set CNC word task of $\geq$ 30% for soft speech (i.e., 50 dBA) in quiet
- N3 (moderate), N4 (moderate/ severe) or N5 (severe) bilateral hearing loss
- Experienced full-time hearing aid users (i.e. >5 hours of use per day for 6 or more months)

The presence of any one of the following exclusion criteria will lead to the exclusion of the subject:

- known allergy to materials in the investigational device
- unable to achieve speech intelligibility scores on an aided open-set CNC word task in quiet with an accuracy of 30% of better for soft speech (i.e., 50 dBA)
- Outside the sp;ecified age range or hearing loss range

8 Measurements and procedures

Hearing aid programming and laboratory testing will be completed in a single 2.5-hour visit with breaks. Test order will begin with CNC word recognition followed by Subjective Comfort/ Preference ratings. Aided CNC word recognition in quiet with SE “off” will be completed first because it will determine eligibility for further aided testing. Unaided CNC word recognition testing at 50 dB HL will be completed next to address the intended use secondary objective even if further aided testing is precluded. Device program order (SE condition) will be otherwise randomized and the “SE off” condition will be repeated to mitigate any potential reduction in score associated with learning the task on first administration. For all tests, program changes will be made by the researcher via the myPhonak or myPhonak Junior app; the Speech Enhancer (SE) condition will be unknown to the participant.

I. Device Fitting and Verification

Children will be fit with study hearing aids matching their personal device form factor; these will be programmed and verified according to DSL v. 5 i/o targets. The start-up program will be changed from the default (AutoSense OS) to Calm Situation. This program will contain speech enhancer “on” at the default (i.e., moderate setting, 14). Two additional programs will be added that are based on “calm”, but with Speech Enhancer strength set to “off” and “strong” (i.e., 20). The Speech intelligibility index (SII), a score between 0.0 and 1.0, that is highly correlated with intelligibility of speech, will be recorded with SE “off”, SE “moderate” and SE “strong”.

II. Speech Recognition

- Stimuli: Speech = CNC words (speech recognition)
- Background:
    - Quiet condition (Ambient noise ≤ 30 dBA)
        - Presentation Levels: Speech = 40 dBA and 50 dBA;
- Hearing Aid Conditions: SE Moderate (14), SE Strong (20), SE Off; Unaided

Speech stimuli will be presented from a single speaker located 1m in front of the listener (Figure 1). One CNC words list will be presented for each condition with no list repetitions.
CNC testing will be completed with SE Off, Moderate and Strong in the following conditions: 40 dBA in Quiet, 50 dBA in Quiet.
CNC testing will also be completed unaided at 50 dBA in Quiet.

III. Comfort Ratings

- Stimuli: The speech stimulus is comprised of looped pairs of International Speech Test Signal [ISTS] sentences (Holube et al., 2010) overlaid with a low-level transient noise track containing sounds such as keyboard typing.
- Background: Quiet (i.e., ≤ 30 dBA ambient room noise)
- Presentation Level: 40 dBA
- HA conditions in randomized order for across participants
    - Speech Enhancer On Moderate
    - Speech Enhancer On Strong
    - Speech Enhancer Off
- Comparisons Conditions: SE Off vs. Moderate; SE Off vs. Strong

Children will perform listening comfort ratings wearing investigational devices. The stimuli will be exclusively presented from a single speaker located 1m in front of the participant. The stimuli are looped identical pairs of ISTS sentences overlaid with looped, low-level identical transient noises. Matched sentence pairs will be played in immediate succession in different hearing aid conditions: SE "off" versus SE "moderate" and SE "off" versus SE "strong". Participants can request to replay sentence pairs before making the following judgments about comfort and preference:

1) Which sounds better?
2) Which is more comfortable?
3) Which do you prefer?

All analysis of the results will occur at the conclusion of the study. Speech scores and subjective questionnaire results will be collected on paper-based forms. Data from these forms will be entered into an electronic spreadsheet prior to data analysis. It will be stored in a secure Hearts for Hearing network folder and a secure folder on a Sonova Sharepoint site

9 Statistical design and analysis

The primary endpoint variable is the percentage correct score on the consonant-nucleus-consonant (CNC) test used to measure speech recognition. Each participant will be evaluated using the CNC test with settings of SE on and SE off in the device. A paired t-test or ANOVA with post hoc comparions will be

performed with the experiment population using these collected measurements, with an assumed two-sided Type 1 Error of 2.5%.

The secondary endpoint analysis is comparison of aided versus unaided performance on CNC words.

10 Investigation Duration

Participant expected duration is approximately 2.5 hours in a one-day appointment. The total expected duration of the investigation is 4 months.

11 Data handling and management

Case report forms will be completed immediately after the lab visit for each participant.
The study team will maintain adequate and accurate study records to enable the conduction of the study to be fully documented and the study data to be subsequently verified. Source documents include, but are not limited to: CIP, List of Essential Study Documents (LoESD), device records, staff curriculum vitae, investigator's notes, questionnaires, visit dates, randomization lists, SAEs, Adverse events (AEs), etc.

The documents (physical and electronic) will be kept on file for 5 years.
During data collection phase of the investigation, physical copies of the data will be compiled and digitized/scanned by the researchers and made accessible to the study manager following each study visit. Data will be reviewed for mis-entries or inaccuracies on weekly or biweekly basis.

An EDC is not applicable for this investigation. Data will be entered into a secure Microsoft Excel spreadsheet, which is located on secure network drive. Only authorized study personnel will have access to the spreadsheet. Only investigators involved in data collection will have authority to enter data.

Participants will be given a participant number to maintain anonymity.

12 Amendments to the CIP

The CIP has been amended based on feedback from the PI and key study personnel. After running one participant they concluded that the battery was too large to be completed in the 2.5 hour planned time frame and that it was very fatiguing for children. Conditions were omitted that were not relevant for study claims including removal of the noise condition (which was initially requested by the PI) and omission of the UWO Plurals test. The primary study objective, involving speech recognition with and without SE, and secondary objective, evaluating hearing aid intended use, were both based on CNC word scores in quiet and all those conditions have been retained. The changes do not influence the data required for claims and reduce overall burden for participants and their families.

13 Deviations from clinical investigation plan

Under emergency circumstances, deviations from the CIP to protect the rights, safety and well-being of the participants may proceed without prior approval by the Sponsor representative (Study Manager), Ethics Commission (EC) and Competent Authority (CA). Such deviations shall be documented and reported to the Sponsor within 2 calendar days, and to the EC and CA within the requisite time frame(s) described below. Apart from that the investigator is not allowed to deviate from this CIP unless that deviation does not influence the investigation data.

14 Device accountability

Study devices must be returned at the completion of the study. A device accountability log will be used to track the investigational devices used during the clinical investigation.

Investigators will enter the serial numbers of devices sent from the Sponsor as well as the dates on which they were received and returned.
If an investigational device has to be replaced due to a device deficiency, the investigator will add the new serial number, device identifier, date of receiving the replacement, date of return of the defect investigational device and mark the returned investigational device as defect on the device accountability log.
In case of device deficiencies, including malfunction, usability issues, or inadequacy in the information supplied by the manufacturer including labelling, the devices will be returned to the sponsor for analysis and the device will be replaced.

15 Informed consent process

Assent and consent will be obtained from participants and parents/ guardians of participants prior to any study participation in accordance with WIRB (EC) guidelines.
For children 6 years of age and younger, no assent is required. Oral assent will be obtained for children 7-11 years of age and written assent will be obtained in children 12-17 years of age. In addition, informed consent forms will be completed by parents/ guardians of all minor participants. All forms must also be signed and dated by the investigator (or their designee) and it will be retained as part of the study records.

16 Adverse events, adverse device effects and device deficiencies

Device deficiencies and all **adverse events (AE)** including all **serious adverse events (SAE)** are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire investigation period, i.e. from participant's informed con-sent until the last protocol-specific procedure, including a safety follow-up period (ISO-14155, 2020). Documentation includes dates of event, treatment, resolution, assessment of serious-ness and causal relationship to device and/or investigation procedure.
Information on AEs is systematically collected during the regular investigation visits, and phone calls (if applicable).
The investigator(s) will follow-up on a biweekly basis with any participant experiencing an AE until either a) the participant reports resolution of the AE or b) 8 weeks have passed since the participant's final visit. If, however, the participant's condition worsens throughout the 8 week follow-up period, the investigator will continue to follow-up biweekly until the AE is resolved or the participant's condition stabilizes over an 8 week period.
The reporting of Serious Adverse Events and Device Deficiencies follows the Regulation (EU) 2017/745 and the MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.
The causality assessment of the SAE will be conducted according to MDCG 2020-10/1 Safety Reporting in Clinical Investigations of Medical Devices under Regulation (EU) 2017/745.

17 Vulnerable populations

This investigational study will include minor children from 4 to 17 years of age.

Assent and consent will be obtained from participants and parents/ guardians of participants prior to any study participation in accordance with WIRB (EC) guidelines.
For children 6 years of age and younger, no assent is required. Oral assent will be obtained for children 7-11 years of age and written assent will be obtained in children 12-17 years of age. In addition, informed consent forms will be completed by parents/ guardians of all minor participants. All forms must also be signed and dated by the investigator (or their designee) and it will be retained as part of the study records.

The WIRB has reviewed and approved all consent and assent forms to confirm they are consistent with ethics committee requirements.

18 Suspension or premature termination of the clinical investigation

The investigation will be suspended or prematurely terminated if the equipment malfunctions or if the participants or investigators are exposed to safety risks other than those outlined in this document. These events may include but are not limited to natural disaster, widespread outbreak of illness, compromised structure of the investigation site, etc.

The blinding code is kept electronically with the study materials. This code can be used to link the participant with their study ID, if needed.
This study is planned for a single session. However, in the event that any participant is asked to return on a separate day, the parent or guardian of the participant will be notified regarding the suspension or premature termination of the investigation via phone call, e-mail or text. If the investigation resumes and the participant is available to resume the study, they will be scheduled for the lab visit.

19 Publication policy

The clinical investigation will be registered in clinicaltrials.gov, a publicly accessible database, as required by U.S. regulations.
The results of the clinical investigation will be published on clinicaltrials.gov no later than one calendar year following the final participant appointment.

The results of the clinical investigation will be summarized in a study report and will be submitted for publication in a peer-reviewed journal. Partial data will be summarized in a Field Study News.
The peer-reviewed journal article will be completed by July 2023, but contingent based on reviewing timeline of the journal and assuming positive decision acceptance.