Study Protocol and Statistical Analysis Plan

Noise Reduction Preferences in Teenagers and Pre-teens

v.2

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Protocol Title

Noise Reduction Preferences in Teenagers and Pre-teens

1 Background

The primary goal for pediatric hearing aid fittings is to maximize speech audi-bility and to mitigate the negative impact of the hearing loss on the child's speech and language development. Research suggests that incidental learn-ing and situational awareness are important for speech and language devel-opment. As such, pediatric hearing aids fittings and feature selection can dif-fer from adults. The potentially unique acoustic environments and listening needs of children must be considered when fitting hearing aids. Balancing au-dibility and comfort by improving SNR with the need for incidental learning has been the challenge for pediatric fittings, and traditionally, such features as di-rectional microphones and noise reduction have been disabled, as these often reduce gain and thereby impact incidental learning, such as which takes place during group work or interactive discussions in the school classroom. However, with developments in noise reduction (as well as directional micro-phones), the audiology community is becoming aware that these features can benefit children and it should not be assumed that enabling and including such features will negatively impact the child's development and/or learning. In fact, several recent publications have espoused the use of these technologies for children. (McCreery,et al 2012; Stelmachowicz, et al 2010; McCreery, et al 2010; Beck 2008; Beck 2014; Pittman 2011).

Special hearing aid features are typically validated and marketed towards the adult population. As many hearing impaired adults have acquired hearing loss following speech and language development, most hearing aid features are recognized as appropriate and beneficial to adults. However, hearing aids de-signed and marketed for the pediatric population typically do not include as many features, mainly because such features are not always appropriate for ideal speech, language, and overall learning development.

Dynamic Noise Cancellation and Tap Control are offered in the newest Phonak devices.

This study aims to identify the preferences of older children (teens and pre-teens) for DNC settings when listening in noise, and if personalization of the DNC feature using the app contributes to reduced listening effort. Subjective preference will be evaluated using blinded A/B comparisons and listening effort will be evaluated using both a subjective slider tool (see Picou, et al 2019) and objective methods (accuracy of words correct and verbal response time for monosyllabic words). Additionally, this study will evaluate speech perception at different DNC settings, from off to strong, which will help inform best practices and recommendations for fittings of older children.

2 Objectives

The primary objective for this study is to determine if DNC "on" at a preferred setting reduces the average *self-perceived* listening effort in teens and pre-teens with mild to severe hearing loss, compared to DNC "off".

The secondary objectives are to determine:
-that DNC "on" at a preferred setting is preferred to DNC"off" when lis-tening in loud noise for teens and pre-teens with mild to severe hearing loss.

-that the majority of teens/pre-teens prefer to use Tap Control to access Bluetooth streaming with their smartphones, compared to using HA push button or phone control.
-that speech intelligibility is maintained with DNC “on”

3 Description of the investigational device

The devices used in this investigation are the Audeo Lumity 90 RICs. The myPhonak app will also be used.
For the purposes of this section, the investigational devices will be considered the hearing aid features of Dynamic Noise Cancellation (DNC) and Tap Control, as these are the specific features being studied for this population. These features are found in the Audeo Lumity devices. DNC is a spatial noise canceller which is currently available on the Audeo Lumity 90 and 70 level devices. The DNC setting is done by the HCP within the Target programming software, or by the end-user via the myPhonak app. The options for setting it range from Off, weak (1-9), moderate (10-16) and strong (17-20).
The overall intended purpose of the device is to amplify and transmit sound ot the ear and thereby compensate for impaired hearing. Tap Control enables the hearing aid user to control the access to streaming from the hearing aids via taps on the ear instead of using physical controls.

4 Design of the clinical investigation

This investigation is a single-group, single site, interventional study. During the lab testing when participants indicate their preference for listening in noise, and during speech perfor-mance testing, they will be blinded as to how the hearing aids are programmed. Participants will serve as their own control as DNC “off” will be a condition in which they are tested.

5 Risks and benefits of the investigational device and clinical investigation

There are minimal risks associated with both the investigational device and participating in the clinical investigation. Identified risks are no greater than those associated with the participants personal hearing aids.
The benefits of participating in the investigation include the possibility of hearing sounds not previously heard, and being able to adjust hearing aids to improve communication in noisy environments. Additionally, participation in this study will help to inform future developments and improvements in hearing device technology for this population.

The research personnel will review these risks with the subjects and answer any questions they have. Hearing aids are not a significant risk investigational device as defined in the FDA 21 CFR 812.3(m).

6 Endpoints

The primary endpoint is listening effort, which is determined by multiple measures from the same dual-task paradigm:

1) **Subjective rating** of the task by answering the question “How easy was it to listen?” using a visual analog scale with verbal anchors at the end points such as “It was very easy” to “It was not at all easy”.

Secondary endpoints will include the following:

1) **Speech Reception Thresholds** is the lowest level, in dB, in which the participant can correctly repeat key words in a sentence. The adaptive HINT-C test will be used with the noise level presented at 67 dB and the target speech signal at varying levels. SRTs will be obtained with the study devices programmed with four different SPiN programs, each one with a different DNC level. The participant's SRT with their own personal hearing aids at their user settings will serve as the control or baseline.
2) **Verbal response time** is the length of time it takes the participant to respond verbally to the monosyllabic words presented in noise, while also performing a visual task simultaneously.

3) **Preferences for DNC "on" compared to "off"** will be measured using a forced choice scale A/B comparison. Hearing aids will be programmed with three different SPiN pro-grams, each one with a different DNC setting (off, weak, strong). Participants will be blinded to the settings.

4) **Preferences for the use of Tap Control** to access BlueTooth streaming from their smartphone will be measured using a subjective questionnaire which will ask participants to rate which method they prefer: Tap Control, HA push button, or phone control.

7 Inclusion and Exclusion Criteria

Inclusion criteria:
-Children, age 10-17
-Mild, moderate, or moderate-severe binaural sensorineural hearing loss
-Native English speakers with ability to communicate verbally
-Able to read and follow directions
-Access to smartphone and willing to download the myPhonak app to personal smartphone
-Experienced hearing aid users (6+ months)

Exclusion criteria:
-Active middle ear infection
-Unable to follow verbal directions
-Unable to communicate verbally
-Unable to tolerate the physical fit of the device

8 Measurements and procedures

All analyses of the results will occur at the conclusion of the study. Speech scores and subjective questionnaire results will be collected on paper-based forms or electronically through use of a lab-owned tablet. Data from these forms will be entered into an electronic spread-sheet prior to data analysis. It will be stored in a secure Vanderbilt network folder and shared with the Sonova once data analysis is complete on a secure Sonova drive in which only the PI has been granted access.

9 Statistical design and analysis

A power analysis on the primary objective was conducted by the PI using G-Power 3.1. Using an expected effect size for this study of 0.7 (see section 6.3) and assuming a two-condition, repeated

measures study with an alpha level of 5% and a power of 80%, 19 subjects would be necessary. Assuming an attrition rate of 20%, the targeted study enrollment for the primary objective would be 23 participants.

Listening effort will be measured by a self-report, subjective question, “How easy was it to listen?” in each condition (DNC “off” and DNC “on” at preferred setting) which will be asked following a dual-task activity. This consists of a primary task of monosyllabic word recognition and a secondary task of a physical response to a visual probe. For purposes of this study, the accuracy of the word recognition will be calculated as well as the verbal response time. A generalized linear statistical model will be used in which the ratings will be the dependent variable, which will be predicted by response time and DNC condition. If there is a significant effect of the DNC condition and the mean ratings are better for DNC on at a preferred setting, the claim that DNC reduces self-perceived listening effort can be substantiated.

A general linear statistical model will also be used to analyze the secondary endpoint of ob-jective listening effort. The dependent variable will be response time, and the independent variables will be the type of response time (either verbal response time in repeating the word or dual task response time of a button press to a colored shape) and also the DNC setting. Random effects of participant and trial will be evaluated if the data can support the complexity of the random effects. The claim of reduced listening effort can be substantiated if the verbal response time is significantly shorter with DNC on than with DNC off.

One sided binomial tests against 50% will be used to determine if the preference for DNC on is significantly different from the preference for DNC off, for the first lab task of listening to speech in a noisy environment. Preference will be measured via a blinded A/B comparison.

Preferences for the use of Tap Control compared to other methods of accessing Bluetooth streaming will also be analyzed using a binomial test.

Deviations from this statistical plan will be documented in the final study report with justification. Possible reasons for deviation include missing data and/or violated assumptions (e.g., vari-ance, distribution, etc).

10 Investigation Duration

This study is expected to take approximately 6 months, but will depend on the recruitment rate. The expected duration for each participant is approximately 2-4 weeks.

11 Data handling and management

Study data is recorded both with paper and with electronic Case Report Forms (p/eCRF). For each enrolled study participant a CRF is maintained. All CRFs are kept current to reflect the subject’s status at each phase during the course of study. Participants cannot be identified in the CRF by name or initials and birth date but an appropriate coded identification is used. All study team members are authorized for the CRF entries and it is assured that any authorized person can be identified both for pCRFs and eCRFs. If pCRFs are used, the investigator’s acronym as well as the subject ID is filled in and data are entered into an electronic file for analysis by the respective investigator and data get monitored by the assigned monitor. In case of a self-evident corrections, either the subject does it by himself or the investigator un-dertakes the correction by crossing out the word/sentence with a single horizontal line and by adding the correction including his personal identifier and the date.

12 Amendments to the CIP

Any necessary amendments to the CIP will be communicated to the study manager/sponsor.
A new version of the CIP will be written, with the necessary changes and justification, and the PI will be trained on the amendments. The amended CIP will go through the approval process and necessary signatures obtained from the study manager/sponsor, PI, and statistician. The amended CIP will be uploaded to the eQMS system as an additional revision.

13 Deviations from clinical investigation plan

Deviations from the CIP to protect the rights, safety and well-being of human participants under emergency circumstances may proceed without prior approval of the sponsor and the EC – such deviations will be documented and reported to the sponsor representative (Study Manager) and the EC as soon as possible. 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

The PI or authorized designee keep records documenting the following in a written process:
• Names of participants who received, used, returned, or disposed of device

• Date of receipt, identification, and quantity of each investigational device (batch/serial number or unique code)

• Expiry date (if applicable)

• Date(s) of use

• Participant identification
If a device needs to be replaced due to a device deficiency, the PI will add the new device serial number, date of receipt, and date of return of the defective device on the Device Accountability Log. In the case of a device deficiency, the Adverse Event/Device Deficiency form will be completed by the study manager and PI together.

15 Informed consent process

At the beginning of the first appointment, investigators will hand the consent form to the par-ticipant and to participant's legal guardian in a private setting and grant sufficient time to read the whole form. The consent form contains detailed information about incentives and reim-bursement. Any questions will be answered and the participant/legal guardian will be given sufficient time to decide whether or not they want to participate in the study. After the partici-pant and legal guardian signs two copies of the consent form, the researcher will sign both copies as well and provide one copy to the participant/legal guardian.

Informed Consent will only be obtained by investigation participants and/or their legal guardians who can provide informed consent themselves before enrollment.

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 following events are to be reported to the Sponsor by the PI (or authorized designee) within 1-2 days after becoming aware of the event:
-Adverse Events
-Serious Adverse Events
- Health hazards that require measures
-Device deficiencies
-Unanticipated Serious Adverse Device Effects
The Sponsor will evaluate SAEs with regard to causality and seriousness. Device deficiencies are also assessed regarding their potential to lead to an SAE (DD with SADE potential).

The following events are to be reported to the Ethics Committee/IRB and to the Competent Authority **within 10 days** by the principal investigator:
- Health hazards that require measures
- Serious Adverse Events

In order to ensure prompt notification, the Sponsor may initially submit an incomplete notifica-tion. The (serious) adverse events will be followed by the PI or Investigator until it has been resolved or until it is recognized as permanent or stable condition. Follow-up may be necessary ac-cording to the study team's medical judgment. In this situation, the follow-up should be docu-mented on the source documents for (serious) adverse events.

17 Vulnerable populations

This investigation includes children age 10-17.

18 Suspension or premature termination of the clinical investigation

The clinical investigation will be suspended or prematurely terminated if the feature and/or investigative device malfunctions or if the participants or researchers 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 investiga-tion site, etc. The trial will be suspended within 5 days of determination that the study or device puts subjects at an unreasonable risk (per 21 CFR 812). The study will be terminated if the participants or researchers are exposed to safety risks other than those outlined in this document.

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.
An internal report of the results of this investigation will be completed and uploaded to the Sonova Quality Management System.
The results of the clinical investigation will be published in an internal study report. The PI will author a submission to a peer-reviewed journal (publication TBD). The internal study report will be available in eQMS.The PI may present results as well to the stakeholders when study is complete.