Protocol

Study Title: Objective response detection to natural speech stimuli for optimisation of hearing aid fitting evaluation

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Background

For people with hearing deficiencies, a specific and well-perceived choice of treatment is of necessity to maintain an optimal quality of life. This step is usually performed by accurately setting up a hearing aid apparatus based on subjective measurements of the hearing impaired's response (e.g. the participant has to provide a physical response when hearing a sound). This assessment cannot be performed with hearing impaired people unwilling or incapable of giving a voluntary response, such as infants or elderly people. For this reason, a myriad of objective assessment tools measuring brain responses to speech stimuli have been proposed (Easwar *et al.*, 2015; Hosseini *et al.*, 2015; Jafarpisheh *et al.*, 2015). A comparative study on how robust these tools would be for hearing aid optimisation has however not yet been performed. Besides this, some tools have only been tested on speech-like stimuli (Easwar *et al.*, 2015; Jafarpisheh *et al.*, 2015), and it would be of interest to assess their applicability to more complex speech stimuli such as sentences or running speech (e.g. from an audiobook). This study proposes to compare the robustness of objective measurements tools for brain responses to speech on a single cohort of hearing impaired volunteers under aided and unaided conditions. The study will be performed by measuring brain responses with a multichannel electroencephalogram (EEG) system whilst the participant is listening to simple or complex speech stimuli. Responses will be measured to clean speech stimuli as well as distorted speech stimuli, e.g. speech in noise. Results of this study could shed further light on how the brain processes speech and give a clear view on the quality of these objective brain response measurements. This could improve the current standards for optimally setting up hearing aid devices.

Research questions:

1. Are speech-evoked objective brain responses sensitive to hearing aid amplification?
2. Are speech-evoked brain responses sensitive to distortions in speech and can hearing aid amplification resolve issues with brain responses to distorted speech?
3. Which (statistical) tests are optimal for detection of objective brain responses to speech?
4. Are realistic speech stimuli (words or running speech) able to robustly detect brain responses compared to current clinical standards (clicks and tones)?

Method

In this exploratory study focussing on the feasibility of obtaining objective measurements of responses to speech under aided and unaided conditions, the research questions will be addressed through a series of experiments in a group of up to 40 participants (in total) with mild to moderate hearing loss in the better hearing ear. Participants will undergo a maximum of two test procedures in which they are exposed to speech or speech-like stimuli (clicks, tones, short phonemes, words, repeated sentences and/or continuous running speech such as extracts from audiobooks). Testing will be performed in a sound treated room.

Materials

Recording of the brain responses will be performed using a 32-channel EEG system (ActiveTwo, BioSemi BV, Amsterdam, Netherlands). System components will be applied as per the manufacturer's recommendations to ensure subject safety and optimal brain response recording. The system has obtained EU health and safety approval to be used for conducting research with human subjects. The experimenters will receive prior training from a member of academic staff experienced with the equipment and closely related protocols. The EEG system uses active electrodes, which means scraping of the scalp is unnecessary. This reduces the discomfort for the participants.

Participants

Participants will be 40 native English speaking subjects aged between 18 and 70 years with mild to moderate hearing loss in their better ear. Participants will be recruited from the hearing impaired cohort at the Royal Berkshire NHS Foundation Trust. Participants that might be suitable for the study will be identified from their medical records. The chief investigator, who is part of their direct healthcare team, will approach the potential participant to offer information about the study. If a participant shows interest in participating after reading the participant information sheet, an audiologist who is part of the participant's medical team will go through the participant information sheet to ensure the participant has no further questions and understands the experiment. Informed consent to participate in the study will be sought by the audiologist. Participation in the study will be entirely voluntary and subjects can be withdrawn at any time without any reason required. Subjects will be informed that they are contributing to research and that they will receive standard care in accordance with current National Institute for Health and Clinical Excellence (NICE) guidelines. Travel reimbursements up to £20 will be made.

Procedure

Experiments will take place at the Royal Berkshire NHS Foundation Trust. As a preparation, subjects will be asked to wash their hair. Before the procedure starts, the researcher performing the experiment will ask if the participant has read the appropriate Participant Information Sheet. Further to this, participants will be asked to complete a questionnaire about their hearing function and any history related to hearing dysfunction. The questionnaire will be sent along with the Participant Information Sheet and will help the researcher to assess if the participant can be included in the study and/or if specific precautions have to be made during the experiment. In the questionnaire, the participant will be asked for his gender, age, native language, current use of medication, presence of neurological diseases,

learning deficiencies, a family history of hearing loss and previous musical training as previous studies have shown that responses to sound stimuli are affected by these characteristics (Hall, 2007). We would also like to ask the participant if he/she hears better from a specific ear as taking measurements from the preferred ear could potentially optimise the responses to speech (Hall, 2007). We will further ask if the participant is aware of skin conditions or allergies as these could increase the chance of an allergic reaction to the electode gel applied on the head for performing the EEG measurement. In case the participant is aware of severe conditions of the skin or allergic reactions, the participant will be withdrawn from the study. In cases of light skin diseases or allergic reactions the researcher will check the skin every 15 minutes to assess if an allergic reaction is occurring. We will ask the participant if he/she is suffering from tinnitus (ringing sound in the ear), current ear discomfort or infection, or has been exposed to noise in the last 24 hours, as these could influence the brain responses or make the test discomfortable for the participant. When deemed necessary, the researcher will delay the test to a later date. Lastly, it will be asked if the participant had any ear surgery as this could lead to incompatibility with the inclusion criteria, and therefore the participant would have to be withdrawn from the study.

Informed consent will be taken from the participant when the researcher has assured the participant understands the experiment and the participant feels any questions related to the study have been answered satisfactorily.

In case their hearing function was not tested within the last 3 months before the first experiment, participants will undergo a standard clinical check-up. We will perform otoscopy on all participants and test the hearing aid of each of the participants using the test battery available at the Royal Berkshire NHS Foundation Trust. The rooms will be set up with appropriate temperature and lighting to ensure subject's comfort. In addition, participants will undergo a speech-in-noise test using the Bamford-Kowal-Bench (B.K.B.) sentence list to obtain a behavioural (subjective) response for detection of speech (Bench *et al.*, 1979). Results of this behavioural test will be compared to objective responses measured as explained below as part of the answer to question 4 of the research questions.

Application of EEG electrodes
An electrode cap appropriate to the subject's head size will be placed on the participant's head whilst ensuring correct electrode placement. After applying an electrolyte gel (recommended by the EEG system's manufacturer) to each electrode holder on the head cap using a clean gel dispenser, pin-type active electrodes will be inserted into these holders. The electrode ribbon cable will be draped over the participants shoulder (to avoid damage and trip-hazards from stepping onto it) and plugged into the Analog-to-Digital Converter (A-D) box. Additionally, individual flat active electrodes will be placed at the forehead and neck to obtain a reference signal. Individual flat electrodes for measuring eye movement will also be applied around the eyes, and one electrode will be placed under the chin to measure muscular activity due to swallowing. Eye and chin electrodes will be used to identify EEG signal segments which contain artefact and need to be removed for further analysis. The individual electrodes will be plugged into individual sockets available on the EEG A-D box.

After checking the impedance of all electrodes are in range of a reference (Common Mode Rejection-Driven Right Leg) electrode to ensure participant safety and data quality, measurement will start. Participants will be asked to sit in a reclining sofa for the measurements and a rolled towel can be provided for neck comfort. Data will be recorded with the software provided by the EEG system manufacturer.

Stimuli

Types of stimuli
Participants will be exposed to three types of stimuli during the test:

1. Short stimuli (tones, clicks or phonemes such as /da/ in Cunningham *et al.*, 2001). These stimuli have been generated for previous research studies at the ISVR to elicit brain responses.
2. Words or Short sentences taken from the B.K.B (Bench *et al.*, 1979), the Hearing in Noise Test (HINT, Nilsson *et al.*, 1994) sentence list or the matrix test developed at Imperial College London by the research group and based on previous research (for review, see Kollmeier *et al.*, 2015). These tests are generally used for assessment of speech perception in noise during hearing tests.
3. Segments of auditory recording from free audiobooks (found on https://librivox.org/ or taken from previous studies at the ISVR and the Institute of Hearing Research) will be used. Audiobook segments have been used in various published research related to speech perception and speech intelligibility analysis (Ding and Simon, 2013).

Stimuli will be presented as clear stimuli or degraded by adding noise at different signal-to-noise ratios (SNRs), or by applying signal processing methods that emulate hearing impairment or speech processing in hearing aids.

Stimulus presentation
Stimuli will be presented at maximally 80 dB (A) through loudspeakers. According to the ISVR Task report on noise and vibration ethics (ISVR Technical Memorandum No. 808, 1996), sound levels must be less than 76 dB (A) for an 8 hour exposure during a 24 hour period, to be considered 'usual'. Participants will undergo sessions where the listening time will be maximally 2 hours at a maximum intensity of 80 dB (A). Stimuli can therefore be considered as usual.

Stimulus levels will be controlled using the calibration procedural approach as per ISO 389-8:2004. These settings of the calibration signal directly control the level of the test stimuli. Calibration will be performed at the beginning of the experimental period and every 4 weeks thereafter.

Test procedure
For this study, participants will be asked to participate in two tests. One of the tests will focus on detecting responses to short stimuli (clicks, phonemes and words). A second test will focus on detecting responses to more complex stimuli (tones, sentences and running speech). Tests will be randomised, and be performed with an interval of at least 24 hours between tests.

<u>Test 1: Short stimuli</u>

After participants are sat in the chair and the EEG electrode are fitted, participants will be asked to listen to click stimuli played from a loudspeaker placed 1 meter directly in front of them. Participants will not wear their hearing aid (unaided condition) for this part of the procedure. This part of the study will take about 10 minutes. Clicks would be considered the gold standard for robustness of response detection and used to answer question 4 of the research questions.

After collecting the click stimuli, participants will be asked to listen to repeated word stimuli under aided and unaided conditions. Word stimuli have been used in previous

experiments with normal hearing participants and showed good detection rate of brain responses. Words will be played as normal and distorted words. Distortions will include high-pass filtered (frequencies above 1000 Hz only) and low-pass filtered (frequencies below 1000 Hz only) versions of the words and words mixed with noise at different signal-to-noise ratios. Each participant will be exposed to 6 conditions listed below, each lasting 7 minutes, in aided and unaided conditions. This means that the total test time will be 12 conditions of 7 minutes, or 84 minutes. Conditions will be randomised during the study. Breaks will be offered between the tests, but researchers will make participants aware they can ask for a break at any time during the procedure. Participants will also be allowed to sleep during this part of the study.

To summarise: the different word conditions are
1. Clean words in quiet
2. Clean words in noise (SNR = 0dB)
3. Clean words in noise (SNR = 3dB)
4. Low-pass filtered words in quiet (0-1000 Hz)
5. High-pass filtered words in quiet (>1000 Hz)
6. High-pass filtered words in quiet (>2000 Hz)

These will be repeated in aided and unaided conditions. This would help in answering questions 1 and 2 of the research questions.

Test 2: Complex stimuli

For this part of the study, participants will be asked to listen to tones and running speech presented from a loudspeaker at 1 meter distance directly in front of them. Running speech will be a segment of about 20 minutes. Participants will be asked to remain attentive during this tests, as we will be measuring cortical responses to speech. To ensure this, they will be asked to answer multiple choice questions regarding the content of the speech presented at random intervals. Participants will perform the experiment twice under aided and unaided conditions. Therefore, at total of 80 minutes of EEG signal to running speech will be collected per participant. Results would be used to answer question 1 and 2 of the research questions.

Lastly, modulated tones will be presented at frequencies of 1000 Hz under aided and unaided conditions at intensities of 40, 60.and 80 dB (A) Tones will be modulated with a modulation frequency of 40 Hz for 6 minutes. Total test time over the entire test 2 procedure will therefore be 92 minutes. For each of the tones, we will ask the participant to rate its loudness on a seven-point scale ranging from very soft to very loud (Castro, *et al.* 2008). This could be used to help answering question 4 of the research questions.

End of experiment
By the end of the recording session all of the equipment, electrodes, insets and cap will be removed gently from the participant by the researcher. Equipment will be cleaned following the manufacturer's recommendations. At the end of the procedures, the experimenter will give information to the participant about the possibility to become part of a database collecting contact information for participants for future studies at the Royal Berkshire NHS Foundation Trust or University of Southampton.

Data analysis
Data analysis will be performed off-line. Pre-processing and artefact rejection will be performed according to current standards in the research field. Data from tests consisting of repeated stimulus sweeps will be averaged over all sweeps to allow analysis of brain responses. For all tests, the relationship of the response to the

speech stimulus will be performed by comparing the stimulus envelope with spectro-temporal features in the (averaged) brain response. Further analysis will include assessment of coherence and delay measurements between EEG channels during brain responses, as well as temporal and spectral assessment tools and source separation techniques.

Statistical analysis

Power calculation
This is a feasibility study, and the research team is only aware of 1 study by Easwar et al (Ear and Hearing. 2015) comparing detection success rate and detection time for words stimuli during aided and unaided listening conditions is available, with only one word stimulus used in this study. The smallest significant difference in response amplitude between aided and unaided conditions at conversational level was 35 nano-volts (nV) with a within-group standard deviation of 30 nV). Based on these findings, the current study would need to include 29 participants for an ANOVA study to have a power of 80% at an alpha level of 0.01. From analysis of cortical responses to running speech in normal hearing participant, we expect larger variability compared to the results found for words, which led us to decide on a participant number of 40.

Statistical analysis of data
Prior to analysing the results, their normality will be tested. This will guide decision on using parametric or non-parametric statistical tests. Temporal relations between responses will be quantified with correlation analysis. Robustness of responses to noise level will be assessed with an F-ratio test. Statistical significant relationships between EEG channels and the stimulus will be tested using analysis of variance measures. Statistical signal processing methods (including bootstrap methods and confidence limits) will be used in detecting responses.

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