Cover Page for Clinial Trial Protocol

Title:

Research protocol: RSRB00073346
Auditory Processing of Complex Sounds – Sensitivity to Chirps
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I. PURPOSE OF THE STUDY AND BACKGROUND

1. **Purpose of the study**.
The purpose of this research project is to study sensitivity of listeners for "chirps," which are fast frequency sweeps that are contained in many natural sounds. We will also test listeners' sensitivity to fast fluctuations in the amplitude, or loudness, of sounds. Based on these results, we will also test novel schemes for processing sounds for potential use in hearing aids. Listeners with normal hearing or with hearing loss will participate.

2. **Background**.
Ongoing physiological and psychophysical studies in our laboratory focus on identifying the features of sounds that are most important for encoding and neural processing of the information in complex sounds. This study will take advantage of that information to test novel strategies for processing sound that may ultimately be used in hearing aids. In this study, we will 1) test listeners for sensitivity to fluctuations in amplitude and frequency within complex sounds, and 2) test novel signal-processing strategies that manipulate the fluctuations in speech sounds.

Note: This study is associated with the next 5-year cycle of an ongoing NIH grant, entitled "Auditory Processing of Complex Sounds." This study has now been categorized as a Clinical Trial by NIH (because listeners with hearing loss will be studied, and we will be manipulating sounds (determined to be an "intervention"). Thus, we are submitting a new protocol and Informed Consent form.

II. CHARACTERISTICS OF THE RESEARCH POPULATION

1. **Number of subjects**. 200 subjects are expected to participate over the 5-year grant duration. We will conduct 4 experiments (see below). For each experiment, our goal is to test 15 listeners with normal hearing (having thresholds within 20 dB of normal), 15 listeners with mild symmetric hearing loss (pure-tone average threshold, PTA, elevated between 20-40 dB), and 15 listeners with moderate symmetric hearing loss (PTA between 40-60 dB). An additional 5 subjects will accommodate attrition and/or subjects who are consented and screened but who do not fit the inclusion criteria (e.g. symmetric hearing loss). Therefore, we will recruit up to 50 subjects for each of the 4 experiments, for a potential upper limit of 200 subjects.
2. **Gender of Subjects.** Approximately 50% of the listeners will be male and 50% will be female.
3. **Age of Subjects**. Listeners will be 18-80 years of age. The auditory tests involved in this study required extended periods of concentration, thus it would not be appropriate to recruit younger or elderly subjects to participate in this study.
4. **Racial and Ethnic Origin**. The racial and ethnic distribution of the subjects will be matched as closely as possible to the distributions in the Rochester community.
5. **Inclusion Criteria**. The inclusion criteria include either normal hearing or mild to moderate sensorineural hearing loss that is similar in both ears, as assessed by a standard

audiogram (hearing test). Additional screening tests will be used to better describe each listener's hearing status, and to ensure that the hearing loss of sensorineural origin.
6. **Exclusion Criteria**. Exclusion criteria are severe (PTA > 60 dB) or asymmetrical hearing loss, as evidenced by a standard audiogram.
7. **Vulnerable Subjects**. No vulnerable subjects will be included in this study.

III. METHODS AND PROCEDURES

1. **Methods and Procedures.**

Human subjects will listen to sounds delivered by headphones and respond using a computer keypad or a mouse. Subjects will be instructed to listen for certain sounds, such as a very brief tone ('beep'), or to speech or music. In some cases, the sound will be presented at the same time as a noisy sound, which makes it more difficult to hear. We will also study responses made for sounds that are changed in different ways using new signal-processing strategies.

Listening sessions will typically last 1-2 hours each, depending on the listener's preference. Sessions can be conducted one or more times a week, depending on the listener's schedule. A total of approximately 3-4 listening sessions is expected for each listener and each experiment, depending on their preferred session duration. Therefore, if a listener opts to participate in all 4 experiments, they may complete up to 16 listening sessions.

We will test the hearing of each listener before the study begins; if listeners have severe hearing loss (greater than 60 dB SPL loss) of which they are not already aware, we will advise them to pursue a professional hearing test and they will be excluded from the study.

In addition to the regular test sessions, each listener will have one additional session dedicated to making a series of three measurements that will allow us to fine-tune our computational model of hearing to each subject. This session will include a standard speech-in-noise test, a tympanogram (to assess middle-ear and Eustachian tube function), and measurement of distortion product otoacoustic emissions (DPOAEs) to assess function of the inner ear. These tests will be conducted with the assistance of Dr. U-Cheng Leong, an audiologist in the Dept. Of Otolaryngology at UR with experience screening subjects for research studies. The speech-in-noise test will be conducted by presenting sounds over headphones and asking subjects to repeat back what they hear. The tympanogram requires placement of a small probe in the ear canal. Measurements of sound pressure in the ear canal will be made in response to a low-frequency tone. During this measurement, the subject may feel an increased sound pressure in the ear canal. This sensation will be described beforehand, so they will know what to expect. The DPOAE measurements will be made by placing small tubes in the ear canal using foam ear plugs. Very small pressures emitted by the ear in response to low-level tones will be measured. These standard hearing tests are not painful or annoying, but simply require the subject to sit still in a comfortable chair during the measurements.

Description of Listening Test sessions (from Grant application):

The sequence of experiments begins with abstract sounds and transitions towards more complex and natural speech sounds.

(Aim 1):

1. Discrimination of complex sounds designed to contain contrasts in amplitude fluctuations and/or frequency chirps. Discrimination thresholds will be assessed for each listener.

(Aim 3):

2. Speech intelligibility tests using synthetic vowels, based on the Klatt (1980) synthesizer. We will manipulate fluctuation contrast, based on models of peripheral responses. These tasks will be performed in quiet and in the presence of a masking noise with spectrum matched to the long-term speech spectrum. The task will identify the lowest contrast at which a given subject can perform at criterion (e.g. > 70% correct for the 12 American English vowels in our test set.) Afterwards, we will also ask listeners to 'manually' adjust the contrast to identify a preferred contrast setting for which clarity of the vowel stimuli is highest.
3. Intelligibility tasks using synthetic consonant-vowel and vowel-consonant syllables constructed using the Klatt synthesizer, with vocal-tract resonances varied to manipulate contrast.
4. The word-in-noise (WIN) task (Wilson et al., 2007). We will initially process these stimuli to enhance contrasts using algorithms implemented in software (Matlab). We will then attempt to implement our algorithms on hardware platforms we are testing as part of the Open Speech project. Intelligibility tests using the hardware processors will be compared directly to those using our software processing. The ultimate goal will be to process running speech with the hardware implementations.

Based on our experience, we anticipate a range in the degree and configurations of hearing loss, and that there will be variability in both the control and SNHL groups in the results of these tasks. Variability across listeners is a strength for our approach, as it allows us to test individualized models in a detailed fashion. Detailed studies of individual listeners can reveal important differences in the performance and cues used between listeners, and within listeners across frequencies (Mao et al., 2015). We plan to test 15 listeners in each of the three groups, for each of the four tasks, for a total of 180 listeners over five years. While we anticipate that many subjects will participate in more than one experiments, we also anticipate that a number of subjects will not satisfy our inclusion criteria or will withdraw from the study for health, scheduling, or personal reasons. Therefore, we anticipate recruiting a total of 200 subjects over five years to successfully complete all of the proposed tests.

If listeners have unusually variable responses during test sessions or fall outside of the expected range of performance, we will explain this difficulty to them, and also coach them and encourage them to focus harder. If that is not successful, and their data are unusable, we will terminate their participation in the study. They will be paid for all time spent as a listener.

The only risk associated with this study is exposure to loud sounds. To minimize this risk, the computer programs that create the sound stimuli will have built-in safeguards to prevent exposure to loud sounds.

2. **Data Analysis and Data Monitoring**

Standard statistical measures (mean, standard deviation) will be applied to the estimated thresholds for detection of small fluctuations in amplitude and/or frequency. Standard measures of speech intelligibility (e.g. percent correct) or of sound quality (e.g. "pleasantness", or "clarity") will be used.

Data Safety & Monitoring Plan

This is a minimal risk study. However, because it was categorized as a Clinical Trial by NIH, we prepared the following Data Safety & Monitoring Plan (from Grant Application):

The Data and Safety Monitoring Plan (Information required by NIH):
Summary Table of Reports: types of reports generated, who they are prepared by, frequency, and their distribution (e.g., IRB, study team, independent monitor/committee)

- Annual reports are submitted by the PI to the IRB. These reports include updated numbers of subjects enrolled, currently being tested, withdrawn from the study, or failed the screening/inclusion criteria.

Process and timeframe for adverse event and serious adverse event captured, assessment types, monitoring, analysis and reporting

- Any unexpected or adverse events are reported in the annual reports submitted to the IRB. Although unlikely in this minimal risk study, if more immediate actions were required in response to an adverse event, the IRB would be contacted immediately.

Process and timeframe for unanticipated event capture, analysis, and reporting

- The PI would identify any adverse events based on reports from our subjects, with whom we work closely. The PI would initiate a report to the IRB.

Process for ensuring data integrity (loss or compromised) monitoring, analysis, and reporting

- Data that is collected on paper forms or in lab notebooks is stored in a locked file cabinet in a locked room. Data that is collected in the form of computer files is stored on an encrypted computer that is backed-up every day into an encrypted server system that the University maintains for research labs, including those that are conducting clinical trials.

For multicenter studies, procedures for ensuring compliance to monitoring plan and reporting across sites

- NA

Human Subjects Protection Training is required for staff.

- The PI and all staff involved in this study have completed Human Subjects Protection Training.
- As this ongoing study may now be categorized as a Clinical Trial, we will now complete Good Clinical Practice (GCP) Training at least every 3 years, per NIH Guide Announcement OD-16-148.

3. **Data Storage and Confidentiality**.

Data is coded by an assigned listener number that is used to identify all computer files and to identify data in plots. The PI will keep the code that relates the listener code to the listener's name in a safe locked place (e.g. in a locked file cabinet inside a locked office.)

This study falls into the newly defined (as of 2018) "Clinical Trial" category of NIH. Therefore, the results of the study will be disseminated on the clinicaltrials.gov website. Subjects will only be identified using their assigned ID numbers.

IV. RISK/BENEFIT ASSESSMENT

1. **Risk Category**. Minimal
2. **Potential Risk**. The risk associated with this study is exposure to loud sound.
3. **Protection Against Risks**. The potential for exposure to loud sound will be minimized by building in safeguards in the computer code that is used to create the sounds.
4. **Potential Benefits to the Subjects**. There are no benefits to the subjects.
5. **Alternatives to Participation**. Subjects can simply elect not to participate in this study.

V. SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT/ASSENT

1. **Method of Subject Identification And Recruitment**.

Subjects will also be recruited using posted flyers that are approved by the RSRB.

2. **Process of Consent**.

The PI or Dr. U-Cheng Leong will obtain consent from listeners. The goals of the study will be described and the listener will be shown the apparatus (headphones or loudspeaker, and computer) and sound-proof booth. Then the listener will be given the opportunity to read the informed consent form and ask questions. A copy of the ICF will be provided to the listener.

3. **Subject Capacity**. Only subjects with the capacity to give informed consent are involved in this study.
4. **Subject/Representative Comprehension**. The PI or Dr. U-Cheng Leong will determine during the initial conversation about the study and/or during the screening test session whether the listener has the capacity to comprehend the goals and risks associated with the study.
5. **Debriefing Procedures**. No information will be withheld from the listener.
6. **Consent Forms**. The consent form is attached below.
7. **Documentation of Consent**. The PI will keep signed consent forms in a safe location (i.e. in a locked file cabinet in a locked office.) A copy of the original signed consent form will be given to the subject.
8. **Costs to the Subject**. The cost of parking or bus transportation will be covered by grant funds.
9. **Payment for Participation**. Listeners will be paid $15/hour for participating in these studies. Payments will be made by check based on the amount of time spent (including partial sessions) after each session.