SUMMARY STATEMENT

PROGRAM CONTACT: [redacted]

(Privileged Communication)

Release Date: **10/28/2020**
Revised Date:

Application Number: **1 R21 DC019217-01A1**
Principal Investigators (Listed Alphabetically): ***Formerly:*** **1R21DC019217-01**

ABEL, TAYLOR JOHN (Contact)
HOLT, LORI L

Applicant Organization: [redacted]

Review Group: **LCOM**
Language and Communication Study Section

Meeting Date: **10/14/2020**
Council: **JAN 2021**
Requested Start: **04/01/2021**

RFA/PA: **PA20-196**
PCC: **HR05**

Project Title: **Flexible representation of speech in the supratemporal plane.**

SRG Action: **Impact Score:13 Percentile:2 +**
Next Steps: **Visit https://grants.nih.gov/grants/next_steps.htm**
Human Subjects: **30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**
Gender: **1A-Both genders, scientifically acceptable**
Minority: **1A-Minorities and non-minorities, scientifically acceptable**
Age: **6A-Children and Adults, scientifically acceptable**

Project Year	Direct Costs Requested	Estimated Total Cost
1	[redacted]	[redacted]
2		
TOTAL	[redacted]	[redacted]

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

1R21DC019217-01A1 Abel, Taylor

RESUME AND SUMMARY OF DISCUSSION: This project will use intracerebral stereoelectroencephalography (sEEG)—and simultaneous scalp electroencephalography (EEG) for comparability to noninvasive measures—in adolescent and young-adult neurosurgical patients to evaluate, using computational modeling, the involvement of different regions of the supratemporal plane in speech perception as the listening context varies. This has the potential for a high impact by shedding light on whether phoneme representation is dynamic or static, a longstanding issue of interest in the speech-perception community, and how context and perceptual weighting factor into any dynamicity. Multiple Principal Investigator (MPI) Abel's expertise in sEEG is well complemented by MPI Holt's experience in auditory cognitive neuroscience, and the research environment is likewise outstandingly well suited for the success of the project. Combining sEEG and scalp EEG is highly innovative and adds a great deal to the generalizability of the project. The proposed tasks are well designed to address the Specific Aims. The resubmission is strengthened by its exceptional responsiveness to the prior critiques, clarifying several points, bolstering evidence of the likelihood of meeting recruitment goals, providing strong preliminary data, and including plans to record from additional brain regions as control conditions. The committee concluded that this work is likely to be completed successfully and to have a sustained, positive influence on the field.

DESCRIPTION (provided by applicant): Speech communication plays a crucial role in conveying our thoughts to others, maintaining social ties, and supporting educational achievement. As a result, communication disorders that impact speech perception like autism, dyslexia, and hearing loss can be costly to both individuals and society. Understanding the neurobiological bases of speech processing is an important goal that has been hastened by invasive intracranial electrophysiology in neurosurgical contexts. Yet, substantial behavioral evidence demonstrates dynamic, flexible aspects of the mapping of speech input to phonemes that is not yet accounted for in neurobiological models. This Exploratory/Developmental R21 project pursues the central hypothesis that listening context systematically impacts cortical response to speech and therefore affects the diagnosticity of acoustic dimensions in signaling phonemes. A newly established cross-disciplinary research team will use intracerebral recording via stereoelectroencephalography (sEEG) obtained in a neurosurgical context to pursue this hypothesis. Like electrocorticography (ECoG), sEEG offers high spatiotemporal resolution and can target the cortical surface, including superior temporal gyrus (STG). Owing to the intracortical electrode placement, sEEG electrodes record through the supratemporal plane, specifically targeting both deep sulcal and gyral grey matter including superior temporal sulcus (STS) and Heschl's gyrus (HG). Simultaneous scalp electroencephalography (EEG) will be acquired to link these intracortical measures with noninvasive approaches appropriate in studies of healthy listeners. Aim 1 will establish neural response to two acoustic-phonetic dimensions as a function of the perceptual weight with which they signal phoneme identity. This will provide a baseline response for each participant for comparison as experimental manipulations to listening context shift perceptual weights in Aim 2, and will establish how individual differences in perceptual weighting strategies predict cortical electrophysiological response. Aim 2 will introduce two well-established manipulations that, behaviorally, shift perceptual weights relative to baseline: introduction of noise and introduction of an 'accent' for which the short-term speech input deviates from distributional regularities of the native language. Examination of experimental manipulations within-participant will provide a sensitive means by which to assay changes in neural response as a function of changes in perceptual weights arising across listening contexts. Participants will be sampled across later adolescence (15-25 years), a period during which perceptual weights provide informative heterogeneity. The project will compound its impact by filling an important gap in understanding of speech processing, building a bridge from invasive electrophysiological studies with patients to scalp EEG measures of human listeners through combined sEEG+EEG, wedding classic and state-of-the-art computational approaches to inform mechanisms, and delivering an

understanding of the dynamic, flexible nature of speech processing with substantial implications for communication disorders.

PUBLIC HEALTH RELEVANCE: The goal of this research is to discover the fundamental mechanisms that support listeners' ability to flexibly perceive speech even as listening contexts change to include foreign accents or background noise. An understanding of how speech perception flexibly adapts will have important implications for developing new rehabilitative strategies for communication disorders like aphasia, dyslexia and autism that impact speech perception.

CRITIQUE 1

Significance: 2
Investigator(s): 1
Innovation: 2
Approach: 2
Environment: 1

Overall Impact: This is a resubmission of an MPI proposal to investigate the variability and flexibility of acoustic dimensions that give rise to phonemic perception and their underlying neural substrates, using stereoelectroencephalography (sEEG) and EEG. The scope of the proposed research is a good fit for the R21 mechanism.

The proposed research will establish the baseline neural responses, and consistent variations, to two acoustic-phonetic dimensions as a function of the perceptual weight with which they signal phoneme identity. The impact is high, since the fundamental perceptual work has been carried out thoroughly by PI Holt, but the neural basis is still poorly understood, and the use of sEEG by PI Abel is very well suited to the task.

The original proposal was strong, and in this resubmission the PIs have been very responsive to reviewer critiques. In addition to clarifying several important points, there are new preliminary data showing 1) strong results obtained using EEG (N=23), which nominally has worse neural sensitivity than sEEG, giving more strength to the proposed number of subjects, and 2) sensitivity to the acoustic manipulations using sEEG (N=7).

1. Significance:

Strengths

- That the acoustic dimensions of VOT and F0 do not contribute to phoneme percept with equal perceptual weights is well established behaviorally but the neural basis is poorly understood.
- How the contributions are reweighted under different acoustic conditions is also well established behaviorally but the neural basis is poorly understood.
- Baseline variability of the weighting across individuals is also not well understood.

Weaknesses

- None noted

2. Investigator(s):

Strengths

- PI Abel, Surgical Director of the Pediatric Epilepsy Surgery Program at Children's Hospital, trained under [redacted] and has strong expertise in sEEG.
- PI Holt has broad expertise in single-unit electrophysiology, animal behavioral models of audition, computational modeling, and human behavioral methods across development. PI Holt developed the stimuli and behavioral paradigms in the proposed project.
- PI Holt has a strong record of mentoring and is co-director of the [redacted]

Weaknesses

- None noted

3. Innovation:

Strengths

- The electrodes will be situated in stereotyped, constrained positions that always include an individual's planum polare, Heschl's gyrus, and planum temporale along the STP.

Weaknesses

- None noted

4. Approach:

Strengths

- The task is well designed, and the framework is an established one.
- The electrodes will be situated in stereotyped, constrained positions that always include an individual's planum polare, Heschl's gyrus, and planum temporale along the STP.
- Strong preliminary data supporting sample size.
- Adding EEG analysis provides a bridge to the far greater number of individuals for whom sEEG is not an option.
- Other recording sites can be analyzed later (or in parallel) for future research.
- The heterogeneity of informative perceptual weights across adolescents and young adults will provide variability that may be explained neurally.

Weaknesses

- The heterogeneity of informative perceptual weights across adolescents and young adults may not be explainable neurally, leading to more unexplainable variance.
- Participants are patients undergoing neurosurgical treatment for medically intractable epilepsy.

5. Environment:

Strengths

- Well-established collaborative environment between CMU and Pitt/Children's Hospital

Weaknesses

- None noted

Study Timeline:

Strengths

- Acceptable

Weaknesses

- None noted by reviewer.

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

- Acceptable

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Acceptable

- Acceptable

Inclusion Plans:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution not justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Not Applicable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically
- Acceptable

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

- The original proposal was strong, and in this resubmission the PIs have been very responsive to reviewer critiques. In addition to clarifying several important points, there are new preliminary data showing 1) strong results obtained using EEG (N=23), which nominally has worse neural sensitivity than sEEG, giving more strength to the proposed number of subjects, and 2) sensitivity to the acoustic manipulations using sEEG (N=7).

Resource Sharing Plans:

Acceptable

Budget and Period of Support:

Recommend as Requested

CRITIQUE 2

Significance: 2
Investigator(s): 2
Innovation: 1
Approach: 1
Environment: 1

Overall Impact: This MPI proposal comes from a phenomenal team, and addresses a novel question: namely how do surface and scalp EEG responses to speech sounds adapt dynamically as a function of the global context they are situated in. The work has relevance for our understanding of individual differences in speech perception generally, and more targeted relevance for mapping the malleability of neural responses to speech in the superior temporal plane. The MPI team has all of the scientific expertise and resources necessary to complete the project, and the project is an ideal scope for this grant mechanism. One notable strength of the proposal is the plan to record scalp EEG in conjunction with intracerebral EEG. This step will allow the team to make concrete links between intra- and extra-cerebral recording. Concerns from a previous round of reviews centered on some details of the analysis plan, and a skepticism that electrode arrays might not contain stimulus-sensitive electrodes. These issues were thoroughly addressed by presentation of new pilot data and fuller explication of the analysis plan. In sum, this is a very strong fundamental science proposal with high innovation and excellent feasibility.

1. Significance:

Strengths

- The question of not only how speech sounds are represented, but how they adapt to shifting acoustic contexts, is highly relevant and novel.
- All too often, invasive intracerebral recording studies provide rich data, but the link between patterns observed intracerebrally and from noninvasive scalp recordings has been opaque. The plan to acquire both measures here will benefit researchers who only have access to non-invasive EEG.

Weaknesses

- This work is fairly far “upstream” from a clinical application. This should be seen as a minor weakness given the theoretical importance of the data to be collected here.

2. Investigator(s):

Strengths

- MPI Abel is a productive early career scientist/clinician. His prior research on the function of the STS, in invasive neural recording, and is an asset to this proposal.
- MPI Holt is a well-respected expert on auditory cognitive neuroscience, with an outstanding research record. Together they have all of the scientific expertise to lead this project.

Weaknesses

- A minor weakness is that this is a new collaboration for the MPI team. This is ameliorated by the presence of collaboratively generated pilot data in the proposal.

- Abel devotes only 0.6 months effort, and it is was not clear that Holt was allocating effort to the project.

3. Innovation:

Strengths

- The use of sEEG to study adaptive placidity to speech is entirely novel.
- Combining invasive and non-invasive methods to find convergence between these types of recording is also very novel.

Weaknesses

- None noted.

4. Approach:

Strengths

- Behavioral paradigms are based on well-established findings from Holt's work.
- Participants will ideally complete all tasks, allowing for interesting analyses of individual differences in response sensitivity across tasks.
- Selection of an adolescent population is likely convenience-based, but offers some interesting avenues for secondary analysis of maturational effects.
- The proposal is supported by promising pilot data using EEG (which is likely less sensitive than the invasive measures to be used), and by feasibility data showing sensitivity of sEEG electrodes in 7 patients to modulations in F0.

Weaknesses

- None noted.

5. Environment:

Strengths

- Children's Hospital of Pittsburgh will be the primary data collection site, and offers all of the clinical resources, workspace, and imaging facilities necessary to carry out the work.
- The MPI's lab at CMU offers resources for behavioral testing.
- The intellectual environment across these locations is excellent.

Weaknesses

- None noted.

Study Timeline:

Strengths

- Timeline seems appropriate and the feasibility of recruiting this sample is supported by caseload numbers provided by the PI.

Weaknesses

- None noted.

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Not Applicable (No Clinical Trials)

Inclusion Plans:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Not Applicable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

- This application was responsive to critiques from a previous round of reviews, specifically by explaining the data analysis scheme in more detail and providing feasibility and pilot data.

Resource Sharing Plans:

Acceptable

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3

Significance: 1
Investigator(s): 1
Innovation: 1
Approach: 2
Environment: 1

Overall Impact: This is an excellent R21 resubmission, in which the MPIs proposed to evaluate the dynamic aspects of speech perception and its neuroanatomical mapping along the supratemporal plane. The research will use intracranial stereo-EEG data from adolescents undergoing invasive epilepsy or oncological diagnostic evaluations. Aim 1 is intended to assess the relationship between

acoustic dimensions and their EEG signatures along the superior temporal gyrus and Heschl's gyrus and Aim 2 focuses on how manipulations of acoustic features reflect in perceptual weight changes in their EEG correlates. The proposal is clearly written, the research is novel and of high significance, the team of investigators has complementary experience in hearing science and neurosurgery, the approach is excellent, and environment is adequate. The investigators have thoroughly addressed the comments from the initial round of reviews, namely related to feasibility, evaluation of extra-temporal regions as controls, specificity of the stimuli and clarifications regarding the methods. They have also included some pilot data to support their responses. One criticism that has remained only partly addressed is the more direct explanation of how the VOT and F0 weights would be mapped onto the EEG data (i.e., a description of the statistical analysis), however, this is a minor concern given the other positive points described above.

Study Timeline:

Strengths

- Adequate

Weaknesses

- None

Protections for Human Subjects:

Acceptable Risks and/or Adequate Protections
Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Acceptable

Inclusion Plans:

- Sex/Gender: Distribution justified scientifically
- Race/Ethnicity: Distribution justified scientifically
- For NIH-Defined Phase III trials, Plans for valid design and analysis: Scientifically acceptable
- Inclusion/Exclusion Based on Age: Distribution justified scientifically

Vertebrate Animals:

Not Applicable (No Vertebrate Animals)

Biohazards:

Not Applicable (No Biohazards)

Resubmission:

- The investigators have thoroughly addressed the comments from the initial round of reviews, namely related to feasibility, evaluation of extra-temporal regions as controls, specificity of the stimuli and clarifications regarding the methods. They have also included some pilot data to support their responses.

- One criticism that has remained only partly addressed is the more direct explanation of how the VOT and F0 weights would be mapped onto the EEG data (i.e., a description of the statistical analysis).

Resource Sharing Plans:

Not Applicable (No Relevant Resources)

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS: ACCEPTABLE

INCLUSION OF WOMEN PLAN: ACCEPTABLE

INCLUSION OF MINORITIES PLAN: ACCEPTABLE

INCLUSION ACROSS THE LIFESPAN: ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Footnotes for 1 R21 DC019217-01A1; PI Name: Abel, Taylor John

+ Derived from the range of percentile values calculated for the study section that reviewed this application.

NIH has modified its policy regarding the receipt of resubmissions (amended applications).See Guide Notice NOT-OD-18-197 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-197.html. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see http://grants.nih.gov/grants/peer_review_process.htm#scoring.

MEETING ROSTER

Language and Communication Study Section
Biobehavioral and Behavioral Processes Integrated Review Group
CENTER FOR SCIENTIFIC REVIEW
LCOM
10/14/2020 - 10/16/2020

Notice of NIH Policy to All Applicants: Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-14-073 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-073.html and NOT-OD-15-106 at https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-106.html, including removal of the application from immediate review.

CHAIRPERSON(S)

[redacted]

MEMBERS

[redacted]

















[redacted]

SAFF[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

SCIENTIFIC REVIEW OFFICER

[redacted]

EXTRAMURAL SUPPORT ASSISTANT

[redacted]

* Temporary Member. For grant applications, temporary members may participate in the entire meeting or may review only selected applications as needed.

Consultants are required to absent themselves from the room during the review of any application if their presence would constitute or appear to constitute a conflict of interest.