AWARD NUMBER: W81XWH-20-1-0485

TITLE: Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Post-deployment Environments

PRINCIPAL INVESTIGATOR: Lee M. Miller

CONTRACTING ORGANIZATION: University of California, Davis, CA

REPORT DATE: July 2021

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE July 2021	**2. REPORT TYPE** Annual Report	**3. DATES COVERED** 01Jul2020-30Jun2021

4. TITLE AND SUBTITLE Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Post-deployment Environments	**5a. CONTRACT NUMBER**
	5b. GRANT NUMBER W81XWH-20-1-0485
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) Miller, Lee M. E-Mail: leemiller@ucdavis.edu	**5d. PROJECT NUMBER**
	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of California, Davis 1850 Research Park Dr., Ste 300 Davis,CA 95618-6153	**8. PERFORMING ORGANIZATION REPORT NUMBER**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012	**10. SPONSOR/MONITOR'S ACRONYM(S)** USAMRAA - CDMRP
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Fitness-for-duty requires good hearing and speech communication ability, especially in complex and noisy environments. But despite its crucial role in operational performance, medical and support personnel have no means to rapidly and reliably assess the integrated functioning of the auditory-speech processing system, either in the clinic or in forward remote settings. Furthermore after deployment, over a million Veterans with Service-related hearing disability – many of whom are older as well – struggle to understand speech in noisy environments such as work meetings or family gatherings, leading to a cascade of physical and mental/emotional health decline. However, because auditory dysfunctions are complex and multi-leveled they remain largely "hidden" audiologically. Measures using simple sounds and detection-threshold tasks, which inform the present US Army H1-H4 fitness-for-duty profile, fail to predict speech comprehension and job performance in Service members. For this profound military operational need, no assessment tool exists. This research will validate a powerful new EEG diagnostic – applicable in austere deployed settings – to assess auditory dysfunction as related to hidden hearing loss and central auditory processing disorders (US Patent No. 10,729,387). Our rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech to differentiate multiple levels of dysfunction from the auditory periphery to cognition, including how these levels interact. This will enable quick screening of Service members in the field for auditory combat-readiness.

15. SUBJECT TERMS

fitness-for-duty, hearing loss, EEG

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC
a. REPORT Unclassified	**b. ABSTRACT** Unclassified	**c. THIS PAGE** Unclassified	Unclassified	56	**19b. TELEPHONE NUMBER** *(include area code)*

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1. INTRODUCTION:

Fitness-for-duty requires good hearing and speech communication ability, especially in complex and noisy environments. But despite its crucial role in operational performance, medical and support personnel have no means to rapidly and reliably assess the integrated functioning of the auditory-speech processing system, either in the clinic or in forward remote settings. Furthermore after deployment, over a million Veterans with Service-related hearing disability – many of whom are older as well – struggle to understand speech in noisy environments such as work meetings or family gatherings, leading to a cascade of physical and mental/emotional health decline. However, because auditory dysfunctions are complex and multi-leveled they remain largely "hidden" audiologically. Measures using simple sounds and detection-threshold tasks, which inform the present US Army H1-H4 fitness-for-duty profile, fail to predict speech comprehension and job performance in Service members. For this profound military operational need, no assessment tool exists. This research will validate a powerful new EEG diagnostic – applicable in austere deployed settings – to assess auditory dysfunction as related to hidden hearing loss and central auditory processing disorders (US Patent No. 10,729,387). Our rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech to differentiate multiple levels of dysfunction from the auditory periphery to cognition, including how these levels interact. This will enable quick screening of Service members in the field for auditory combat-readiness. Our Specific Aims include: AIM 1: Relate objective measures of hearing ability – from the brainstem through cognition – to relevant behavioral measures of operational performance (comprehension, ignoring distractions) and readiness (listening fatigue). AIM 2: Establish the test-retest reliability of the measures, within individual listeners over time (months to years). This will enable an "Early Warning" system to detect any decline in listening ability. AIM 3: Demonstrate that non-specialists can use the test to classify fitness-for-duty with durable, off-the-shelf hardware and minimal training in noisy or remote environments.

2. KEYWORDS:

hearing loss, speech perception, auditory dysfunction, fitness-for-duty, selective attention, audiology, electroencephalography, EEG, auditory brainstem response, ABR, speech tracking

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**

The major goals and timeline that overlap with this period of the project are shown below. (Note that several timeline entries extend into the second and third award period.) As detailed below, all human subjects-related goals were severely impacted by the COVID-19 related research shutdown:

	Proposed Timeline	**Completion Date**	**% Complete**
Specific AIM 1: Performance-based neurobehavioral fitness-for-duty classifier	Months		
Milestone Achieved: Local IRB Approval	0	7/8/2020	100%
Milestone Achieved: HRPO Approval	4	6/30/2021	100%

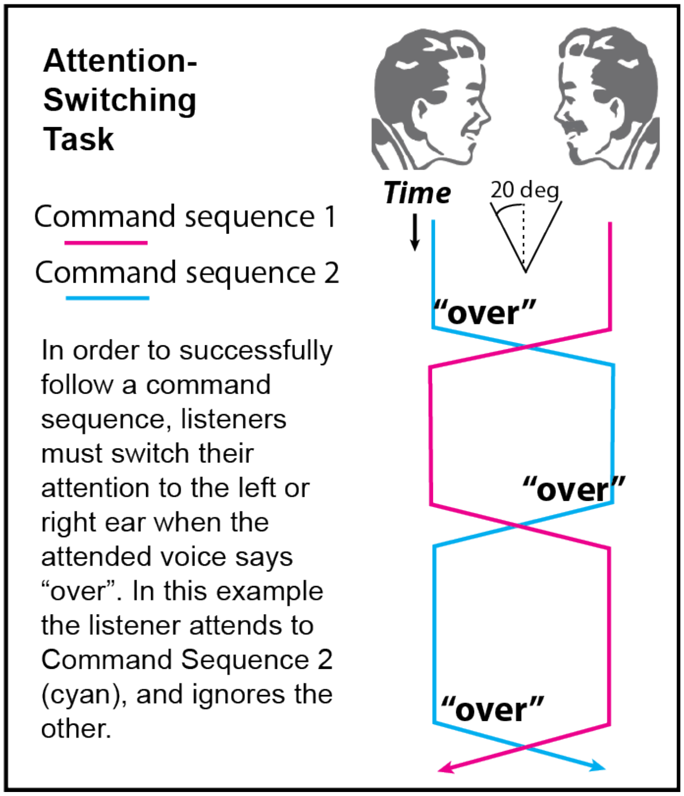
Develop experimental stimuli	1-3	as of 6/30/2021	90%
Pilot EEG-task sessions	4-5	(Begun as COVID-19 shutdown allowed: 6/30/2021)	10%
Audiological Exams	6-24	(Anticipated to commence 10/1/2021)	0%
Behavioral and EEG-task sessions	6-24	(Anticipated to commence 10/1/2021)	0%
Specific AIM 2: Test-retest reliability and "Early Warning" profile			
Audiological Exams, sessions 2-4	2-30	(Anticipated to commence 2/1/2022)	0%
Behavior and EEG-tasks, sessions 2-4	2-30	(Anticipated to commence 2/1/2022)	0%

Despite the COVID-19 research shutdown, we were able to make substantial progress on the following goal well in advance of its proposed timeline.

Specific AIM 3: Non-specialist use in austere environment			
Software development: automated processing framework and intuitive GUI interface	25-27	6/30/2021	70%

- **What was accomplished under these goals?**
  Major activities and significant results
  We achieved significant progress on all project goals that did not require enrolling human subjects: developing the experimental stimuli and behavioral-EEG paradigm, data processing pipeline, and machine learning classifier.

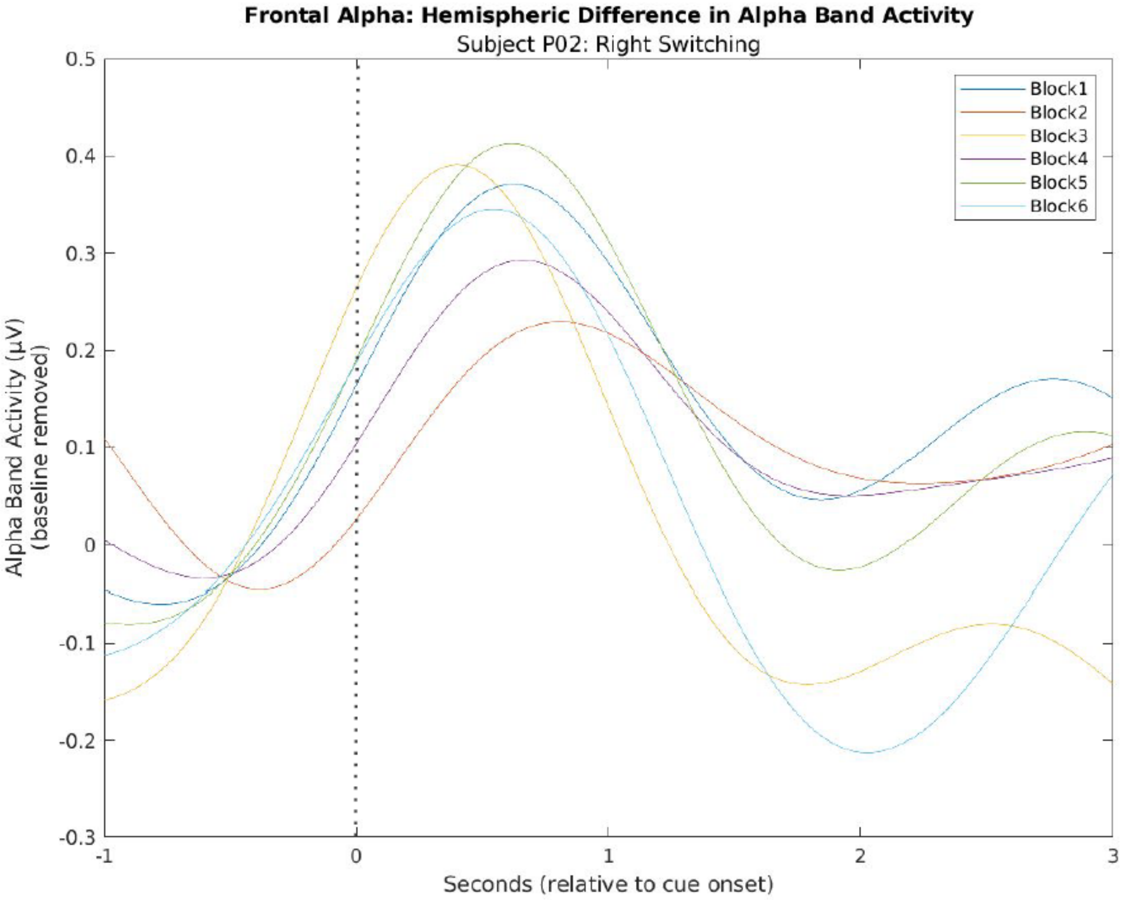
  In the proposed behavioral-EEG paradigm, participants must follow a dynamic conversation with operational instructions and tactical commands, modeled on Army Field manuals and other DoD-related corpuses such as the Speech in Noisy Environments (SPINE2). Listeners must attend to one or the other ear and press a button whenever they hear a target word, which will be contextually relevant but unpredictable and drawn from a phonetically balanced set of the NATO phonetic alphabet (“alpha”, “bravo”, “charlie”, etc.), with a target occurring on average every 10 seconds. Participants are instructed to switch their attention from one ear to the other whenever the attended talker says the switch word “Over”, which occurs every few sentences (avg. 6 seconds). At that moment that ear’s talker continues speaking but with task-irrelevant information*, so the listener must switch attention immediately to continue performing*. This also provides an internal control that each talker is attended for half the time. Furthermore during the entire task, subjects fixate their gaze on one of two printed images of faces positioned at approximately +/-20 degrees from midline in the horizontal plane, corresponding to the attended ear; no video screens are required, for ease of use in austere environments. This allows us to assess the speed of attentional shift in multi-talker conditions using the horizontal EOG signal, which in our pilot work shows slowing with increasing listening fatigue.



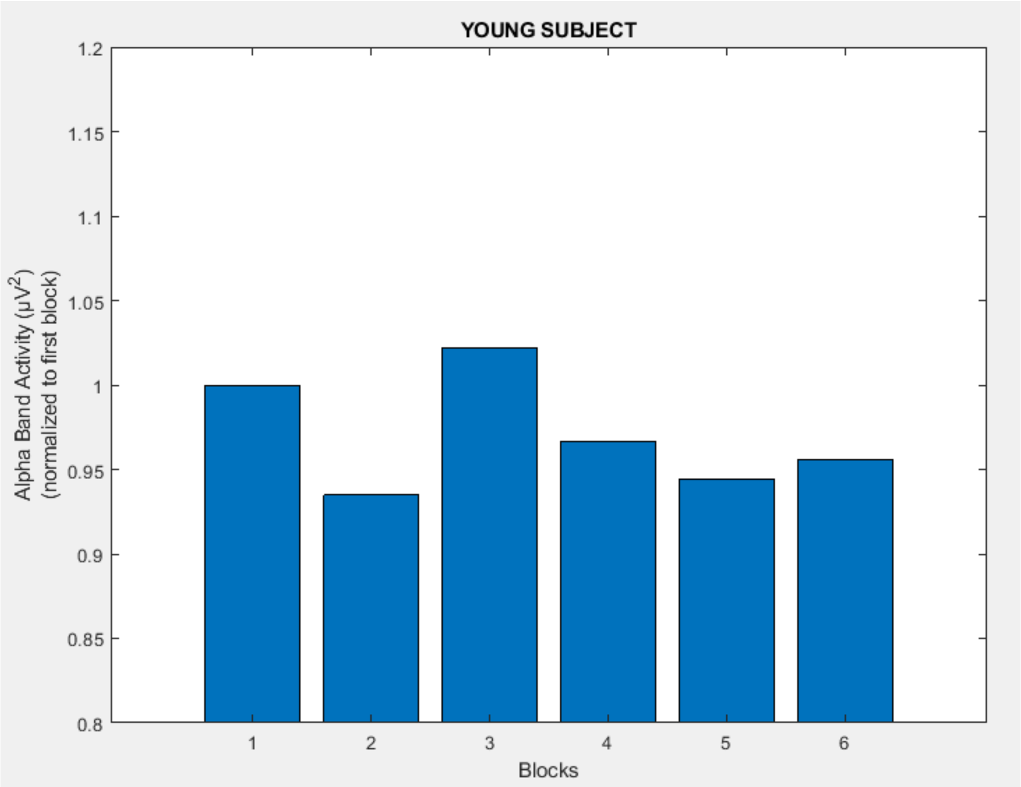
Attention-Switching Task

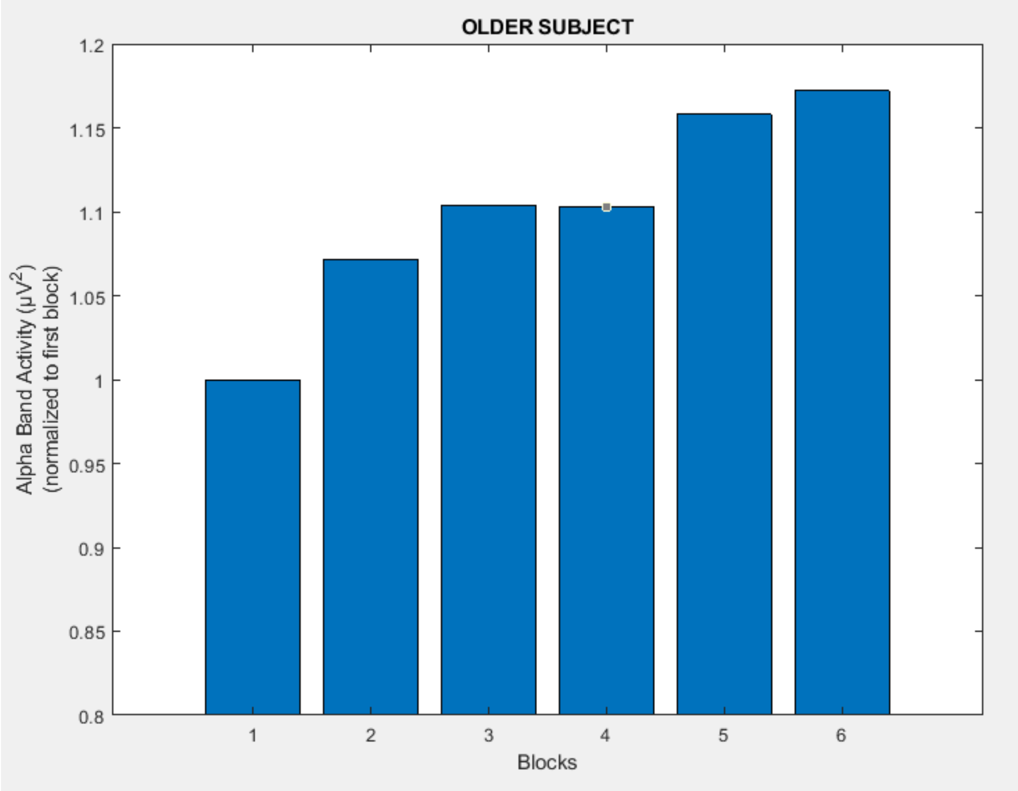
In order to successfully follow a command sequence, listeners must switch their attention to the left or right ear when the attended voice says “over”. In this example the listener attends to Command Sequence 2 (cyan), and ignores the other.

We have completed a pilot version of this paradigm and, as COVID-19 research restrictions began to lift at the end of this reporting period, we were able to acquire high quality EEG and behavioral metrics from pilot participants (fellow researchers). This allowed us to validate the key aspects of the proposed EEG-behavior task. Results include a clear, brain-based metric of a listener’s attentional control in the power of EEG oscillations ~10Hz, also known as alpha power. When a listener switches attention from a talker on the right to a talker on the left, or vice versa, this is manifest in brain signals by a shift of alpha power from one hemisphere to the other. In addition to the magnitude of a neural attentional switch, this alpha hemispheric difference gives precise timing information about how quickly attentional control can engage (e.g. after hearing the cue word “over”). Shown below is the alpha power hemispheric difference in one listener over 6 8-minute blocks separated by short breaks. This demonstrates that our paradigm, as expected, has a powerful effect on the spatial attentional control system, that we can obtain a millisecond-resolution read-out of a listener's attentional switching speed, and that alpha power lateralization should be a highly salient feature in the machine learning model.



Additional results show that older listeners likely fatigue more rapidly as a result of their greater listening effort. This is evidenced by an increase in overall alpha power (as opposed to alpha hemispheric difference) over the course of the recording. The plots below show alpha power in a young subject (left), showing little change over the ~1 hour paradigm. In contrast, a middle-aged listener shows a dramatic *increase* in alpha power over time, correlating with increased fatigue and a likely decline in speech perception performance. This dynamic – which is extremely clear from our brain recordings – will also serve as a key feature in the machine learning classifier for auditory fitness-for-duty.





Finally, we have developed all aspects of the data analysis pipeline up to the feature-extraction step for machine learning. We have also made substantial progress on developing the machine learning classifier model itself. This goal was proposed for a later award period but accomplished early in lieu of human subjects data acquisition (curtailed by COVID-19). As proposed, the classifier algorithm we use is Support Vector Machine (SVM). However in addition to specifying the algorithm and any hyperparameters, one must also take care to choose the appropriate features for the model. In our case, with such rich and high-dimensional behavioral, audiological, and EEG data, our potential feature space is vast and – in many cases – highly collinear. We have therefore been developing a Genetic Algorithm for feature selection that works in tandem with the SVM. With this approach, we expect to achieve a classifier with maximum selectivity and specificity while maintaining high computational efficiency.

Stated goals not met: Goals not met are enumerated in the SOW chart above and are strictly limited to those impacted by the COVID-19 research shutdown. We estimate that although the COVID-19-related research shutdown delayed our human subjects data acquisition by approximately 10 months, we were able to accomplish goals from latter portions of the SOW in advance. Thus we estimate our overall SOW delay from the COVID-19 shutdown will be much less, with the goal of realigning the budget and milestones in early Y22-23.

- **What opportunities for training and professional development has the project provided?**
  The project is not primarily framed as a training and professional development opportunity, however research of this kind inevitably serves that purpose – particularly for junior researchers. During this reporting period, our lead Research Specialist completed training in machine learning through a graduate course in Spring 2021 (Neuroscience 211: "Advanced Topics in Neuroimaging").

- **How were the results disseminated to communities of interest?**
  The patent awarded on Aug 4, 2020 is freely available to the public at https://www.google.com/patents/WO2016011189A1?cl=en (Miller, L.M., B.D. Moore. Frequency-multiplexed speech-sound stimuli for hierarchical neural characterization of speech processing, U.S. Patent No. 10,729,387.)

  Our peer-reviewed publication, which describes the EEG speech tracking technique that will be central to our machine learning classifier for auditory fitness-for-duty, appears in the premier, high profile cognitive neuroscience journal (Beier E, Chantavarin S, Rehrig G, Ferreira F,. Miller LM. (2020) Cortical tracking of speech: Towards collaboration between the fields of signal and sentence processing. J Cog Neurosci 33(4):574-593.)

  Professor Miller delivered an Invited Presentation describing our ongoing work at the UC Davis Dept. Otolaryngology / Head & Neck Surgery, Annual Research Symposium (6/18/2021), which was attended by local and regional researchers and clinicians.

- **What do you plan to do during the next reporting period to accomplish the goals?**
  Our Office of Research has recently allowed campus research to approach pre-COVID-shutdown protocols. Furthermore we have all necessary project personnel coming on board in the next 5 weeks (Aug 1 and Sept 1, 2021). As a result, we will rapidly realign with the proposed SOW timeline, and plan to complete 83% of behavioral and EEG-task sessions (100 Veterans) in the next reporting period.

4. **IMPACT:**

- **What was the impact on the development of the principal discipline(s) of the project?**
  This research is likely to significantly advance toward clinical/field application the first and only auditory fitness-for-duty assessment that validates operational performance and readiness for active-duty Service members. This novel assessment tool will have immediate, profound impact on Service member team safety, communication, and effectiveness in dynamic and noisy environments.

  Our listening diagnostic builds on years of careful research by our lab and many others, but real world impact depends as much on practical implementation as it does on the underlying science: if an auditory fitness-for-duty assessment can only be conducted in a large hospital or laboratory by highly trained personnel, its impact will be sorely limited. Our approach is uniquely designed from the outset for the broadest possible application, through its speed, portability, robustness in austere or adverse environments, and ease of use by non-specialists. Our proposed research will validate all these attributes, demonstrating that inexperienced individuals with only one hour of training can conduct the assessment rapidly and reliably.

  The method is equally applicable in post-deployment Veterans, many of whom suffer from lasting service-related auditory injury. Here, the method's speed and ease of use will also impact its utility, bringing the tool within reach not only of large VA hospitals but also small private audiology practices and local, non-specialized clinics.

- **What was the impact on other disciplines?**
  Beyond the operational and post-deployment impact on military personnel and their families, in the long term our approach has the potential to transform restorative hearing health care globally, ultimately improving care for the half a billion people worldwide who have hearing loss. Every day these individuals struggle to understand speech, particularly in noisy conditions, leading to billions of dollars in lost productivity (in the US alone, hundreds of billions annually) and, too often, a tragic and costly cascade of social, psychological, and physical decline. The challenge is that a listener's difficulty understanding speech in real life stems not only from problems in the ear, but from how each individual's brain processes sounds. For decades, our capable audiology providers and hearing device manufacturers have struggled to enact effective, individualized hearing care because they lack the means to rapidly and reliably assess the integrated functioning of the auditory system in a life-relevant context. As a result, they are limited in how to guide treatment. For instance hearing aids and other devices are often poorly matched to an individual's impairment, and aids often fail in the situations where listeners need them most: e.g. restaurants, business meetings, family gatherings. Moreover, nascent cellular and molecular treatments for hearing loss (e.g. hair cell restorative drugs) also lack an objective, multileveled metric of therapeutic impact. For this profound global health problem and frank scientific-industrial need, no clinical assessment tool has ever existed. Our ongoing research will finally provide it.

- **What was the impact on technology transfer?**
  Granting of the core patent underlying our approach (8/4/2020) represents a significant step toward technology transfer. We expect this technology to have a commercial impact, either through a startup and/or licensing agreements. As we obtain human subjects data in Y21-22, our Office of Research will prepare a regulatory approach with UC Davis Tech Transfer office, including any premarket applications to the FDA, will help apply for funding to conduct any anticipated trials necessary for classification and clearance, and will contact potential industry partners.

- **What was the impact on society beyond science and technology?**
  The work is likely to have a substantial impact on society and employment by improving the audiological treatment, social integration, and work productivity of those with hearing loss. Since hearing loss leads to a cascade of mental and physical impairments (social isolation, depression), the research promises to ameliorate many of these costly downstream effects as well.

5. **CHANGES/PROBLEMS:**

- **Changes in approach and reasons for change**
  Nothing to Report.

- **Actual or anticipated problems or delays and actions or plans to resolve them**
  As noted above, human subjects research at UC Davis was shut down due to the COVID-19. Presently, this is being resolved and our Office of Research is now allowing operation under near-pre-Covid protocols.

- **Changes that had a significant impact on expenditures**
  Delays due to the COVID-19 research shutdown led to a temporary reduction in expenditures, in particular delays in hiring staff and human subjects costs (subject payments, audiological exams). One graduate student assisted part time on the experimental paradigm. The budgeted Research Specialist onboarded in June 2021 and the two budgeted Postdoctoral Fellows will be starting Aug 1, 2021 and Sept 1, 2021. We were however able to purchase the major equipment – a Brain Products EEG system – so there was no impact on expenditures in that category.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**: None.
- **Significant changes in use or care of human subjects**: None
- **Significant changes in use or care of vertebrate animals:** N/A
- **Significant changes in use of biohazards and/or select agents**: N/A

6. **PRODUCTS:**

- **Publications, conference papers, and presentations**
  Invited presentation at the UC Davis Department of Otolaryngology / Head and Neck Surgery Research Symposium (18 June, 2021).

- **Journal publications.**

Beier E, Chantavarin S, Rehrig G, Ferreira F,. Miller LM. (2020) Cortical tracking of speech: Towards collaboration between the fields of signal and sentence processing. J Cog Neurosci 33(4):574-593.
Published.
Acknowledgment of federal support: **Yes**

- **Books or other non-periodical, one-time publications.** Nothing to Report.
- **Other publications, conference papers, and presentations.** Nothing to Report.

- **Website(s) or other Internet site(s)**
  At this stage we are not yet disseminating data and results to the scientific community. This will commence when we acquire human subjects data in Y21-22.

- **Technologies or techniques**
  We have begun developing the machine learning model that will serve as the core of our auditory fitness-for-duty classifier (see section *Accomplishments* for details). We will make all Research Resources publicly available in accordance with CDMRP expectations, as expressed in the General Application Instructions, Appendix 2, Section K.

- **Inventions, patent applications, and/or licenses**
  PATENT awarded on Aug 4, 2020: Miller, L.M., B.D. Moore. Frequency-multiplexed speech-sound stimuli for hierarchical neural characterization of speech processing, U.S. Patent No. 10,729,387 . https://www.google.com/patents/WO2016011189A1?cl=en

- **Other Products**
  Our novel behavioral-EEG paradigm and the EEG data analysis pipeline are nearly complete, and our machine learning classifier is under active development.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

Name:	Lee M. Miller
Project Role, etc.:	PI (no change)

Name:	Hilary Brodie
Project Role, etc.:	co-PI (no change)

Name:	Britt Yazel
Project Role:	graduate student

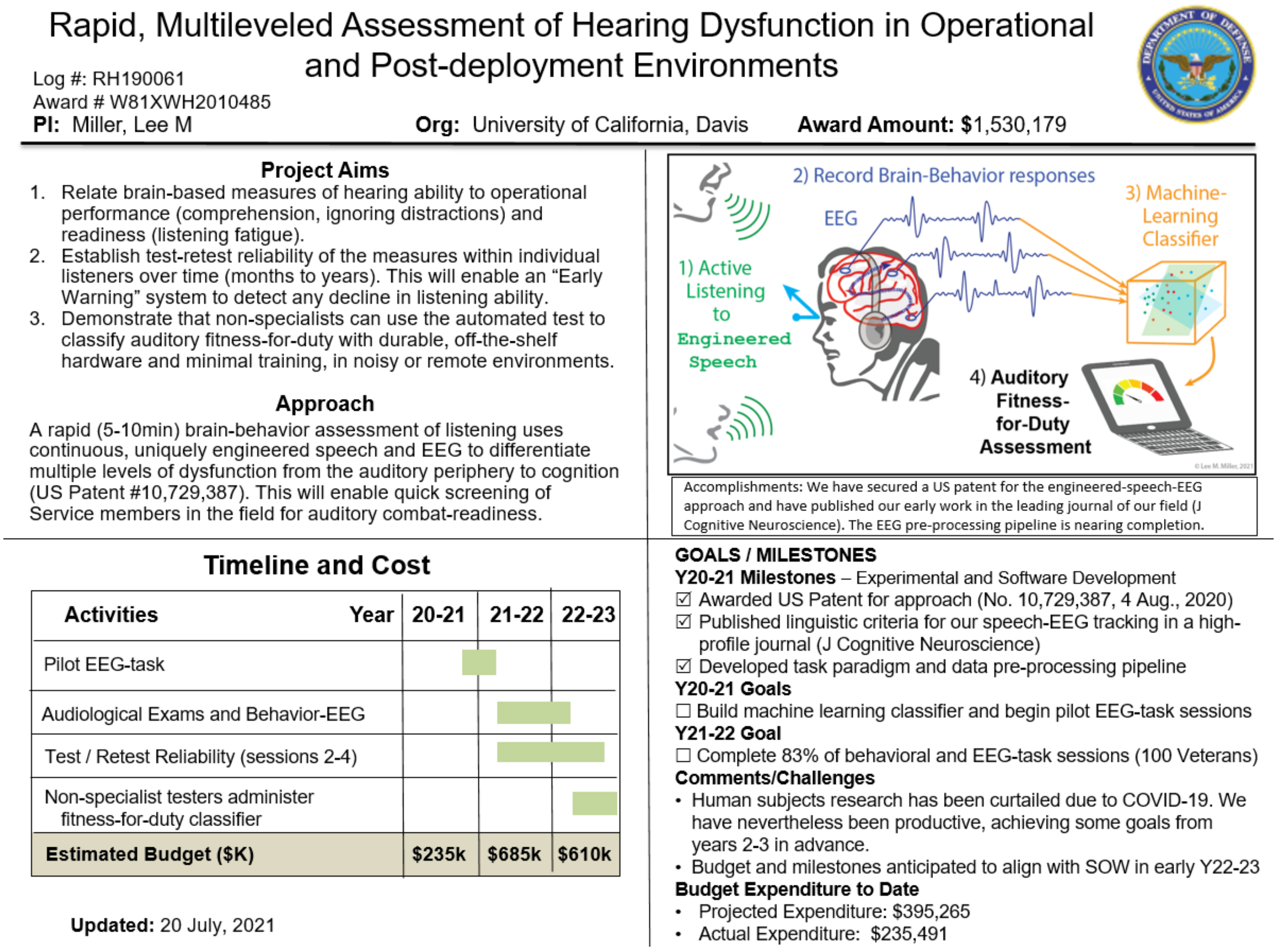
Researcher Identifier (ORCID ID):	none
Nearest person month worked:	2.5
Contribution to Project:	Mr. Yazel worked to develop the behavioral-EEG task.
Funding Support:	Remaining funding during the academic Y20-21 was provided through Teaching Assistantships

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
  One active grant **closed** since the last submission of other support:
  5 R01-DC014767 (Corina and Miller) 07/01/2015 - 06/30/2020 2 calendar
  NIH/NIDCD (annual direct)
  Grants officer: Christopher Myers <cm143g@nih.gov
  Determinants of Cross Modal Plasticity in Children with Cochlear Implants
  This project assesses the determinants of cross-modal plasticity in a pediatric population of deaf children with cochlear implants in an effort to promote successful language outcomes.
  Role: Co-PD/PI

- **What other organizations were involved as partners?**
  Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

o QUAD CHART:



Rapid, Multileveled Assessment of Hearing Dysfunction in Operational and Post-deployment Environments

Log #: RH190061
Award # W81XWH2010485
PI: Miller, Lee M
Org: University of California, Davis
Award Amount: $1,530,179

Project Aims

1. Relate brain-based measures of hearing ability to operational performance (comprehension, ignoring distractions) and readiness (listening fatigue).
2. Establish test-retest reliability of the measures within individual listeners over time (months to years). This will enable an "Early Warning" system to detect any decline in listening ability.
3. Demonstrate that non-specialists can use the automated test to classify auditory fitness-for-duty with durable, off-the-shelf hardware and minimal training, in noisy or remote environments.

Approach

A rapid (5-10min) brain-behavior assessment of listening uses continuous, uniquely engineered speech and EEG to differentiate multiple levels of dysfunction from the auditory periphery to cognition (US Patent #10,729,387). This will enable quick screening of Service members in the field for auditory combat-readiness.

Accomplishments: We have secured a US patent for the engineered-speech-EEG approach and have published our early work in the leading journal of our field (J Cognitive Neuroscience). The EEG pre-processing pipeline is nearing completion.

Timeline and Cost

Activities Year	20-21	21-22	22-23
Pilot EEG-task	🟩	🟩	
Audiological Exams and Behavior-EEG		🟩	🟩
Test / Retest Reliability (sessions 2-4)		🟩	🟩
Non-specialist testers administer fitness-for-duty classifier			🟩
Estimated Budget ($K)	**$235k**	**$685k**	**$610k**

Updated: 20 July, 2021

GOALS / MILESTONES

Y20-21 Milestones – Experimental and Software Development

☑ Awarded US Patent for approach (No. 10,729,387, 4 Aug., 2020)
☑ Published linguistic criteria for our speech-EEG tracking in a high-profile journal (J Cognitive Neuroscience)
☑ Developed task paradigm and data pre-processing pipeline

Y20-21 Goals

☐ Build machine learning classifier and begin pilot EEG-task sessions

Y21-22 Goal

☐ Complete 83% of behavioral and EEG-task sessions (100 Veterans)

Comments/Challenges

- Human subjects research has been curtailed due to COVID-19. We have nevertheless been productive, achieving some goals from years 2-3 in advance.
- Budget and milestones anticipated to align with SOW in early Y22-23

Budget Expenditure to Date

- Projected Expenditure: $395,265
- Actual Expenditure: $235,491

9. APPENDICES:

I. (PATENT) Miller, L.M., B.D. Moore. Frequency-multiplexed speech-sound stimuli for hierarchical neural characterization of speech processing, U.S. Patent No. 10,729,387 . https://www.google.com/patents/WO2016011189A1?cl=en

II. (PUBLICATION) Beier E, Chantavarin S, Rehrig G, Ferreira F,. Miller LM. (2020) Cortical tracking of speech: Towards collaboration between the fields of signal and sentence processing. J Cog Neurosci 33(4):574-593.

United
States
of
America

To Promote the Progress of Science and Useful Arts

The Director

of the United States Patent and Trademark Office has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this United States

Patent

grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America, and if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States of America, products made by that process, for the term set forth in 35 U.S.C. 154(a)(2) or (c)(1), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b). See the Maintenance Fee Notice on the inside of the cover.

Andrei Iancu

DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE

Maintenance Fee Notice

If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number and timing of the maintenance fees required may be changed by law or regulation. Unless payment of the applicable maintenance fee is received in the United States Patent and Trademark Office on or before the date the fee is due or within a grace period of six months thereafter, the patent will expire as of the end of such grace period.

Patent Term Notice

If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, 365(c), or 386(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.

US010729387B2

(12) **United States Patent**
Miller et al.

(10) **Patent No.: US 10,729,387 B2**
(45) **Date of Patent: Aug. 4, 2020**

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(54) FREQUENCY-MULTIPLEXED SPEECH-SOUND STIMULI FOR HIERARCHICAL NEURAL CHARACTERIZATION OF SPEECH PROCESSING

(71) Applicant: **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA**, Oakland, CA (US)

(72) Inventors: **Lee Miller**, Davis, CA (US); **Bartlett Moore, IV**, Houston, TX (US)

(73) Assignee: **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA**, Oakland, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/406,047**

(22) Filed: **Jan. 13, 2017**

(65) **Prior Publication Data**

US 2017/0196519 A1 Jul. 13, 2017

Related U.S. Application Data

(63) Continuation of application No. PCT/US2015/040629, filed on Jul. 15, 2015.

(Continued)

(51) **Int. Cl.**

A61B 5/00	(2006.01)
A61B 5/0484	(2006.01)
A61B 5/0476	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/741*** (2013.01); ***A61B 5/0476*** (2013.01); ***A61B 5/04845*** (2013.01)

(58) **Field of Classification Search**

CPC G06F 3/011; G06F 3/015; A61N 1/36036; A61N 1/36; A61N 1/08; A61N 1/36171;

(Continued)

(56) **References Cited**

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4,275,744	A	6/1981	Thornton
4,593,696	A	6/1986	Hochmair et al.

(Continued)

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EP	2581038	A1	4/2013

OTHER PUBLICATIONS

Dau, T. et al., "Auditory brainstem responses with optimized chirp signals compensating basilarmembrane dispersion." J Acoust Soc Am 107(3): 1530-1540, Mar. 2000.

(Continued)

Primary Examiner — Deborah L Malamud

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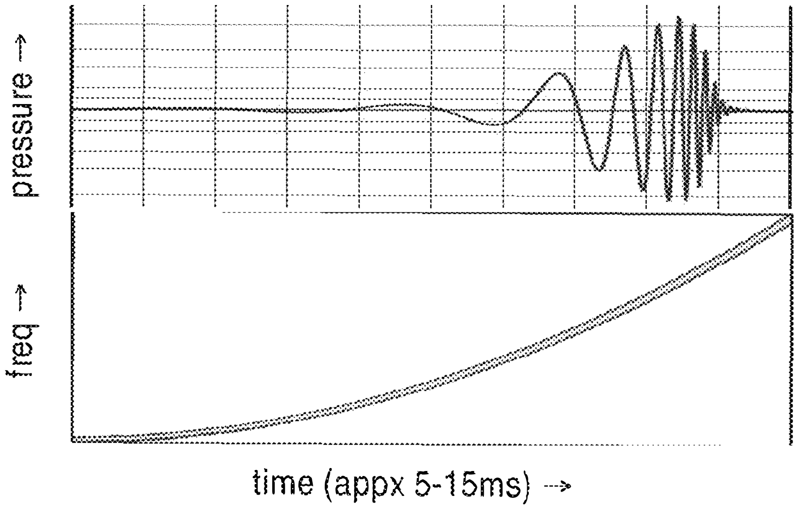
(57) ABSTRACT

A system and method for generating frequency-multiplexed synthetic sound-speech stimuli and for detecting and analyzing electrical brain activity of a subject in response to the stimuli. Frequency-multiplexing of speech copora and synthetic sounds helps the composite sound to blend into a single auditory object. The synthetic sounds are temporally aligned with the utterances of the speech corpus. Frequency multiplexing may include splitting the frequency axis into alternating bands of speech and synthetic sound to minimize the disruptive interaction between the speech and synthetic sounds along the basilar membrane and in their neural representations. The generated stimuli can be used with both traditional and advanced techniques to analyze electrical brain activity and provides a rapid, synoptic view into the functional health of the early auditory system, including how speech is processed at different levels and how these levels interact.

20 Claims, 5 Drawing Sheets



Related U.S. Application Data

(60) Provisional application No. 62/024,646, filed on Jul. 15, 2014.

(58) **Field of Classification Search**
CPC A61N 1/36196; A61N 1/36034; H04R 25/606; H04R 25/505; H04R 25/305; H04R 25/353; A61B 5/0476; A61B 5/0482; A61B 5/04845; A61B 5/4064; A61B 2562/0204; A61B 5/0006; A61B 5/0042; A61B 5/121; A61B 5/4836; A61B 5/4848; A61B 5/486; A61B 5/7267; A61B 5/741; H04S 7/307
See application file for complete search history.

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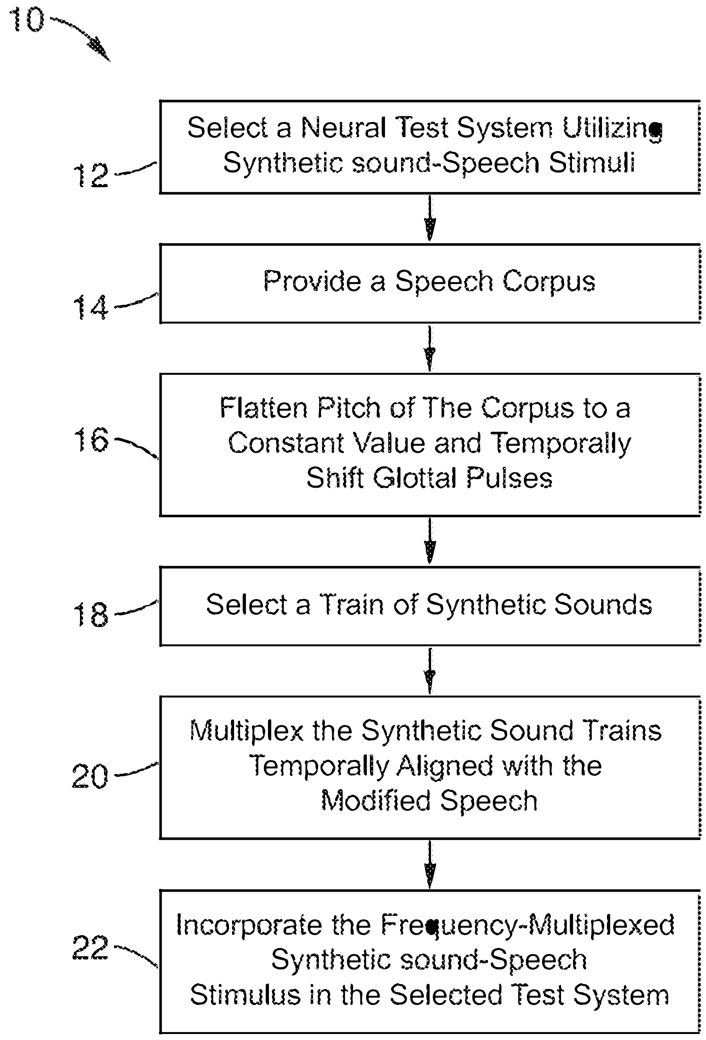
10
12
Select a Neural Test System Utilizing Synthetic sound-Speech Stimuli
14
Provide a Speech Corpus
16
Flatten Pitch of The Corpus to a Constant Value and Temporally Shift Glottal Pulses
18
Select a Train of Synthetic Sounds
20
Multiplex the Synthetic Sound Trains Temporally Aligned with the Modified Speech
22
Incorporate the Frequency-Multiplexed Synthetic sound-Speech Stimulus in the Selected Test System

FIG. 1

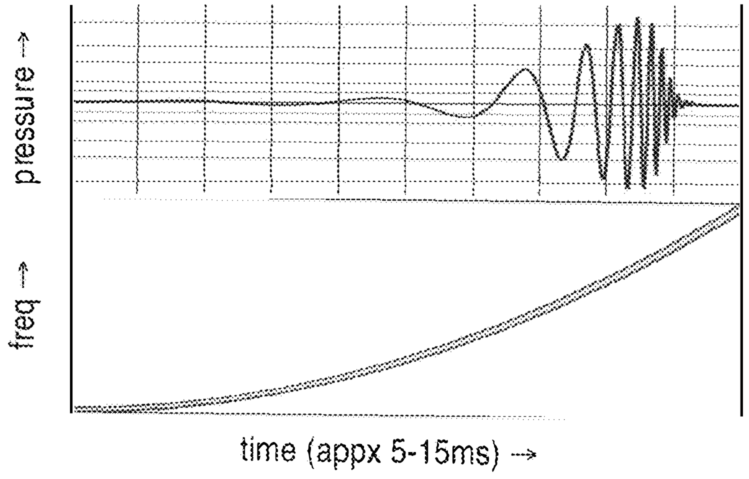
pressure →
freq →
time (appx 5-15ms) →

FIG. 2

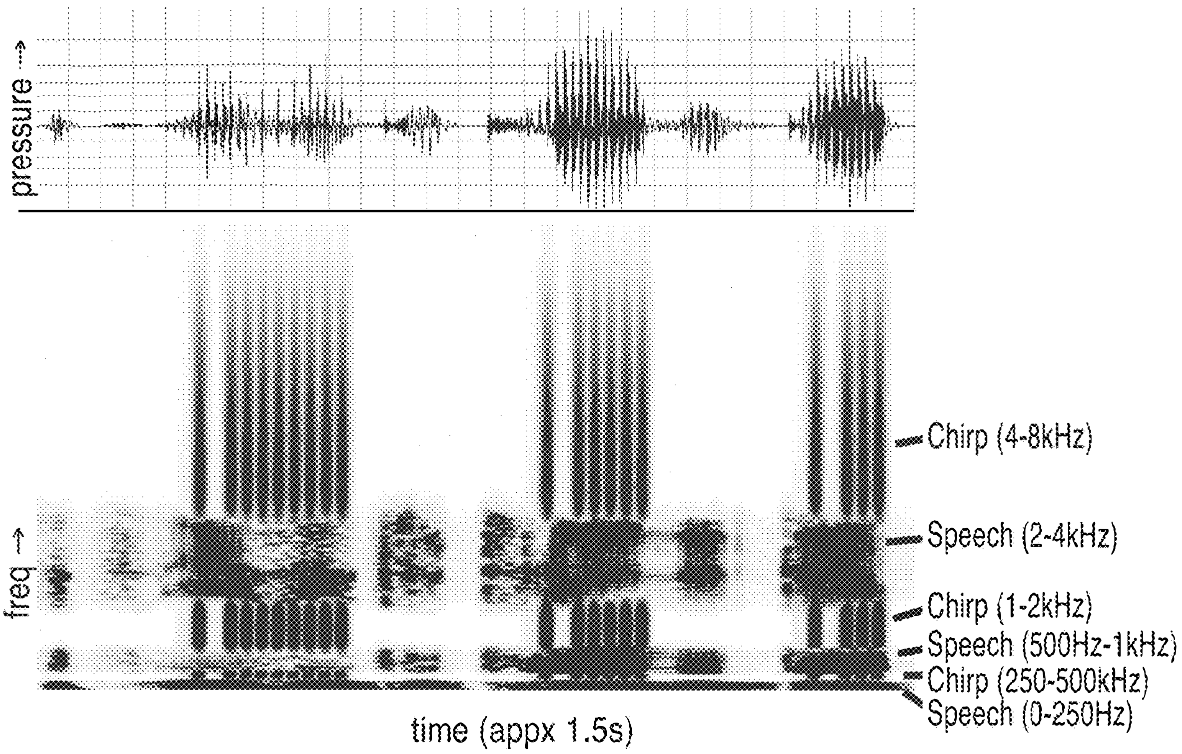
pressure →
freq →
Chirp (4-8kHz)
Speech (2-4kHz)
Chirp (1-2kHz)
Speech (500Hz-1kHz)
Chirp (250-500kHz)
Speech (0-250Hz)
time (appx 1.5s)

FIG. 3

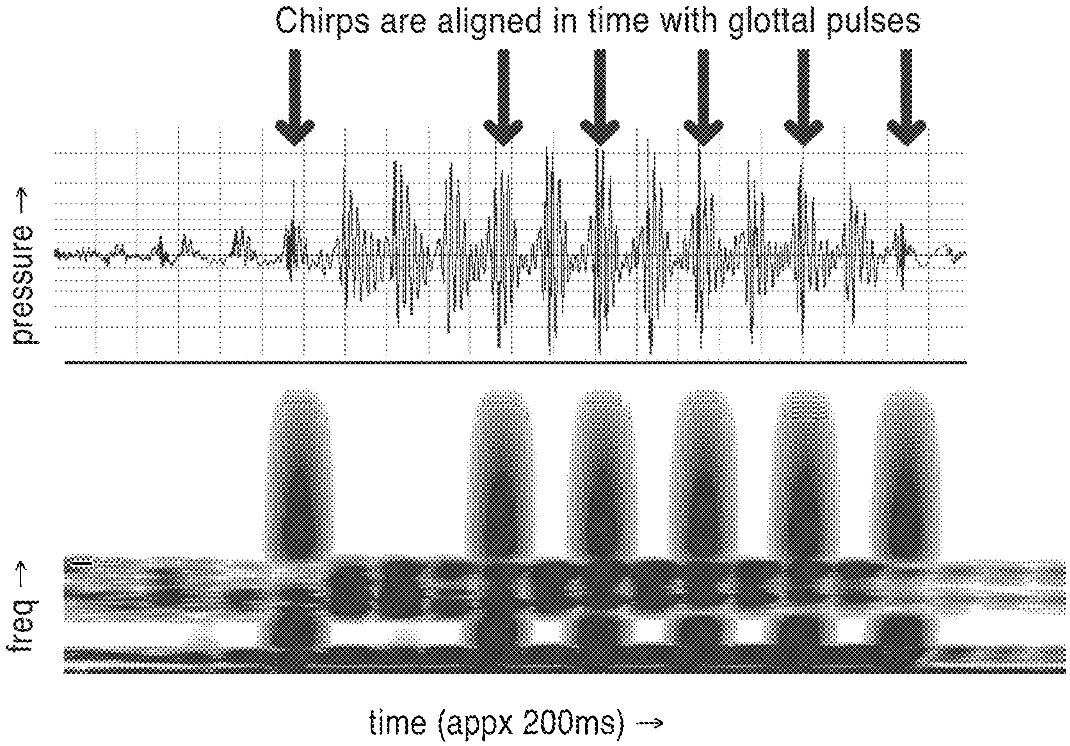
Chirps are aligned in time with glottal pulses
pressure →
freq →
time (appx 200ms) →

FIG. 4

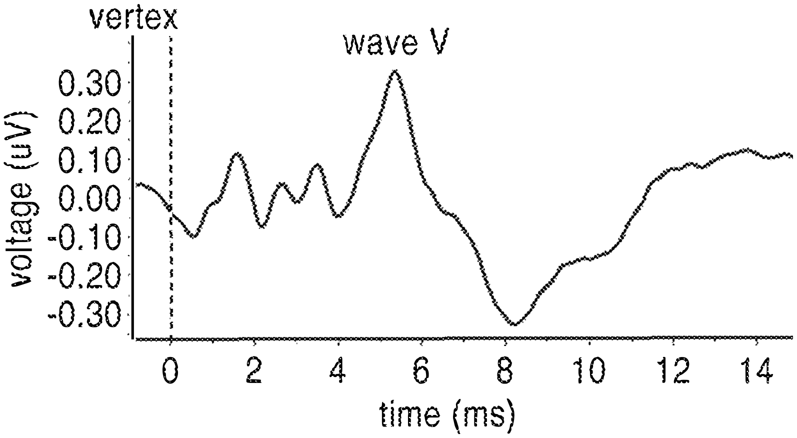
vertex
wave V
voltage (uV)
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
0
2
4
6
8
10
12
14
time (ms)

FIG. 5

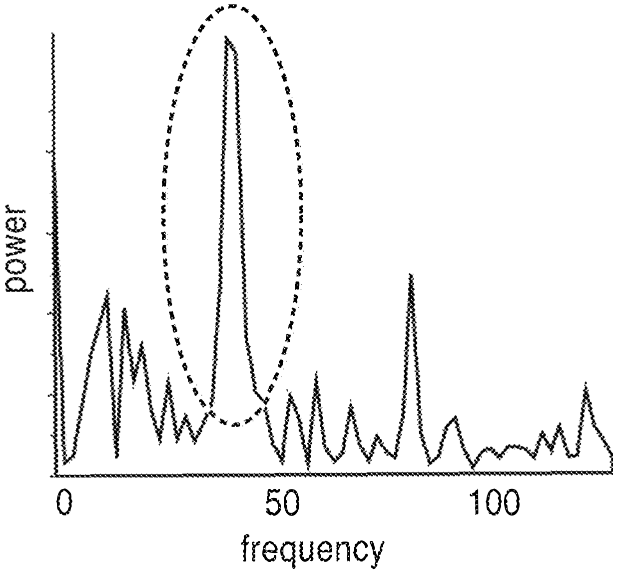
power
0
50
100
frequency

FIG. 6

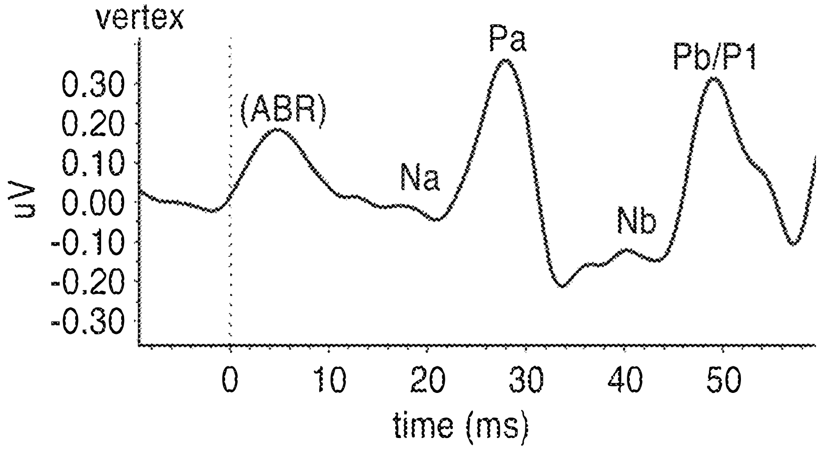
vertex
Pa
Pb/P1
(ABR)
Na
Nb
uV
0.30
0.20
0.10
0.00
-0.10
-0.20
-0.30
0
10
20
30
40
50
time (ms)

FIG. 7

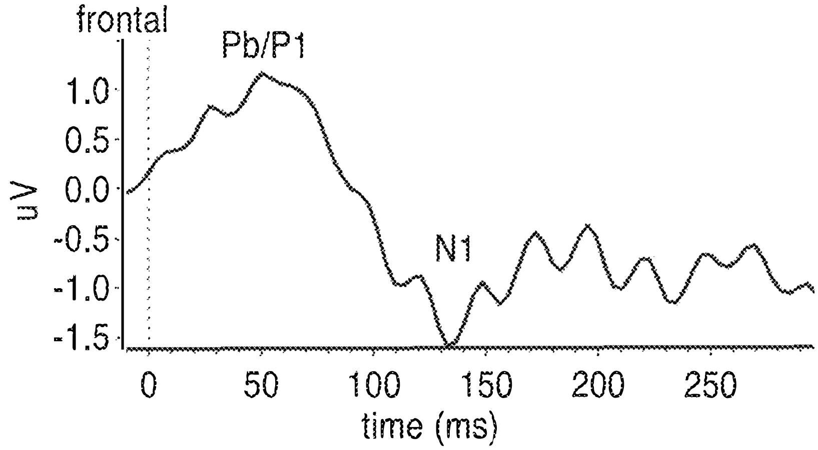
frontal
Pb/P1
N1
uV
1.0
0.5
0.0
-0.5
-1.0
-1.5
0
50
100
150
200
250
time (ms)

FIG. 8

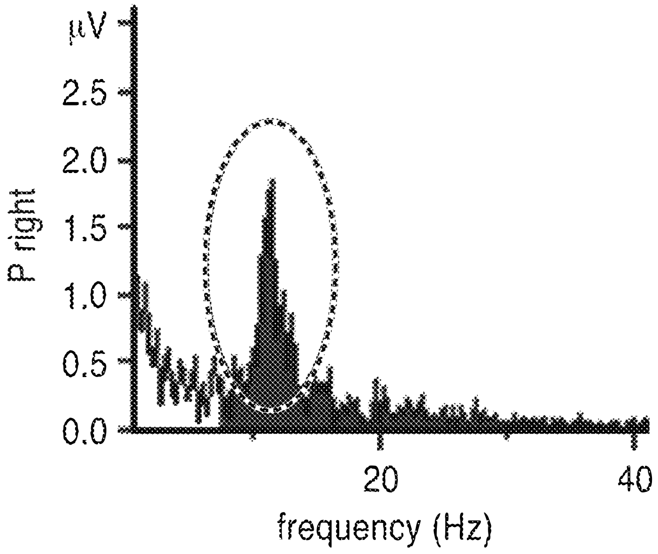
μV
2.5
2.0
1.5
1.0
0.5
0.0
P right
20
40
frequency (Hz)

FIG. 9

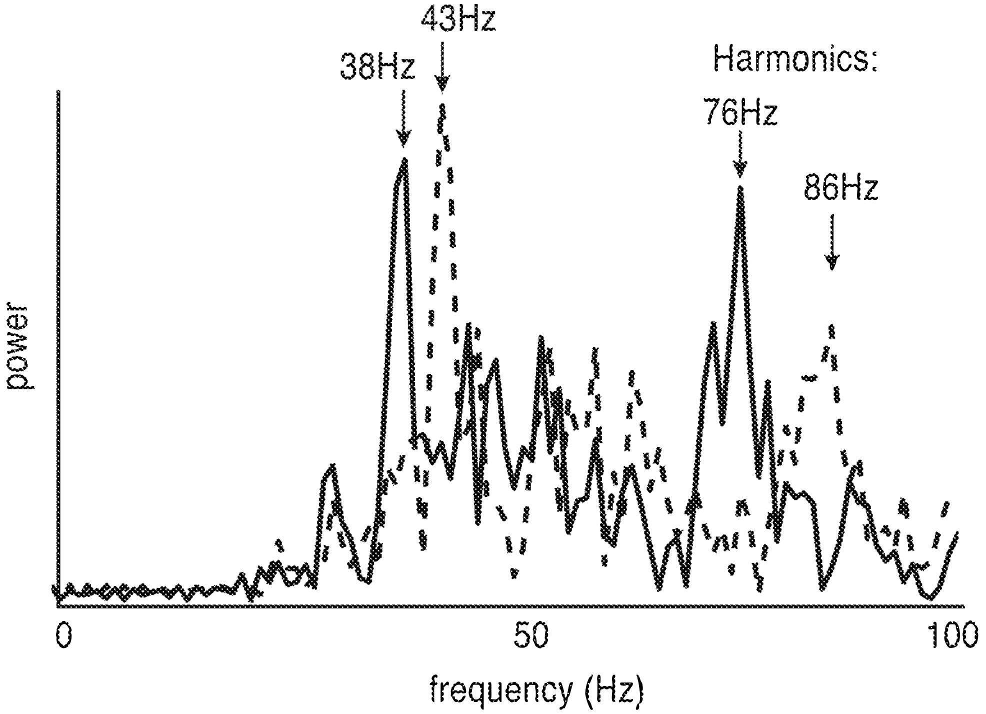
43Hz
38Hz
Harmonics:
76Hz
86Hz
power
0
50
100
frequency (Hz)

FIG. 10

FREQUENCY-MULTIPLEXED SPEECH-SOUND STIMULI FOR HIERARCHICAL NEURAL CHARACTERIZATION OF SPEECH PROCESSING

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a 35 U.S.C. § 111(a) continuation of PCT international application number PCT/US2015/040629 filed on Jul. 15, 2015, incorporated herein by reference in its entirety, which claims priority to, and the benefit of, U.S. provisional patent application Ser. No. 62/024,646 filed on Jul. 15, 2014, incorporated herein by reference in its entirety. Priority is claimed to each of the foregoing applications.

The above-referenced PCT international application was published as PCT International Publication No. WO 2016/011189 on Jan. 21, 2016, which publication is incorporated herein by reference in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

This invention was made with Government support under DC008171, awarded by the National Institutes of Health. The Government has certain rights in the invention.

INCORPORATION-BY-REFERENCE OF COMPUTER PROGRAM APPENDIX

Not Applicable

NOTICE OF MATERIAL SUBJECT TO COPYRIGHT PROTECTION

BACKGROUND

1. Technical Field

The present technology pertains generally to auditory stimuli and detecting electrophysiological signals in response to the stimuli, and more particularly to producing frequency-multiplexed chirp-speech stimuli that can be used with both traditional and advanced techniques to analyze electrical brain activity.

2. Background

Medical diagnosis and treatment of auditory system diseases and deficiencies have been advanced with an increased understanding of the integrated functions of the auditory system components. Generally, sounds presented at the eardrum are transmitted through the three bones of the middle ear to the oval window of the auditory inner ear called the cochlea. The movement of the oval window by the stapes bone pushes and pulls on the enclosed fluid of the cochlea creating compression pressure waves travelling

approximately at the speed of sound in water. The motion of the fluid in the cochlear tubes also generates travelling waves along the length of the basilar membrane.

Sensory receptor cells, called hair cells, are positioned on an epithelial ridge on the basilar membrane called the organ of Corti. Motion of the basilar membrane of the cochlea activates the auditory receptor cells (hair cells) sitting on the membrane which send signals through the auditory nerve to the brainstem. The nerve signals activate more neurons and the auditory messages are sent to the midbrain, thalamus, and on to the auditory cortex of the temporal lobe of the cerebrum.

The cochlear travelling wave travels much slower than sound travels in water and peaks at frequency specific locations along the length of the basilar membrane. The basilar membrane is not uniform throughout its length and is relatively narrow but thick at the base and is relatively wide and thin at the apex of the cochlea. As a consequence of the structure, a cochlear travelling wave has a peak amplitude or height of displacement of the basilar membrane at a certain point along its length that is determined by the frequency of the sound that originally produced the motion of the cochlear fluid. High frequencies cause a peak wave near the narrow part of the membrane at the base and low frequencies produce their peaks toward the apex at the broad part of the membrane. The receptor cells on the basilar membrane may also be tuned to particular frequencies, so that each cell responds best to a sound of a given frequency.

The motion of the travelling wave of the basilar membrane is from the base up to the maximum point of displacement and then quickly fades. The latency of the traveling wave is quite short at the base, in the range of tens to hundreds of microseconds, but lengthens dramatically for peak displacements near the apex of the basilar membrane with latencies in the range of 10 ms or greater.

The traveling wave has been considered the fundamental mechanism for analysis of sounds in the cochlea since it was found that the traveling wave amplitude grows linearly with sound intensity and shows a broad peak near the resonant frequency location in the cochlea.

However, a time delay is observed from the initial auditory stimulus at the tympanic membrane and the neural activity produced in the auditory nerve or in the brain stem. It is also observed that the latency to the firing of auditory nerve fibers is comparatively shorter for fibers that are tuned to high frequencies and longer for fibers tuned to lower frequencies.

This latency is caused, in part, by frequency-dependent traveling wave delays. Because a traveling wave takes a period of time to reach from the base to the apical end of the cochlea, the corresponding receptor cells and fibers of the auditory nerve are not stimulated simultaneously. Consequently, synchronization between the nerve fibers is decreased due to the delays introduced by the traveling wave. The temporal dispersion or asynchrony of the collective output from the different neural elements results in a reduction of the amplitude of the corresponding compound neural response (e.g. ACAP or ABR).

The temporal asynchrony between the neural elements can be partially compensated for with a short auditory stimulus such as an upward chirp, where the higher frequencies are delayed relative to the lower frequencies. By aligning the arrival time of each frequency component of the stimulus, the chirp stimulus can shorten the latency and shift the waves. Essentially, the structure of the stimulus can influence the deflections of the basilar membrane and the corresponding timing of the stimulation of the hair cells of the basilar membrane and auditory nerve of the inner ear.

Auditory stimuli such as clicks, chirps or tone pulses have become part of several different procedures in the auditory field such as the auditory brain stem response (ABR), auditory compound action potential (ACAP), and the auditory steady-state response (ASSR). For example, hearing screening in newborns based on auditory brainstem response (ABR) is a well established method for the early detection of hearing impairment.

Several models have been developed that attempt to capture the major features of cochlear behavior. Nevertheless, there are many aspects of the human auditory system that are not fully understood. For example, it is not understood how different features of a sound, such as frequency, intensity, or onset and offset that are carried to higher brain centers separately through parallel nerve pathways are interpreted by the cerebral cortex.

Speech is perhaps the most important stimulus that humans encounter in their daily lives. Unfortunately, certain populations have difficulty understanding speech, particularly in noisy conditions, including children with language-based learning problems and users of cochlear-implant/hearing-aids. Even in the hearing impaired, much of this difficulty stems not from problems in the ear itself, but from how each individual's brain processes the speech sounds.

Considering its importance, audiology clinics devote little effort to the neural processing of continuous speech from the ear to auditory cortex. Currently there is no way to rapidly and reliably assess the integrated functioning of the auditory system from brainstem to cortex. For this profound, global health problem, no clinical assessment tool exists. Accordingly, there is a need for devices and methods that will allow the diagnosis, treatment and study of human hearing.

BRIEF SUMMARY

The present technology provides synthetic sound-speech stimuli and a method for creating sound-speech stimuli that can be used with both traditional and advanced techniques to analyze electrical brain activity. The synthetic sound-speech stimuli used in conjunction with suitable diagnostic systems can provide a wide variety of assessments as well as experimental procedures for medical practitioners and researchers. For example, it will provide a rapid, synoptic view into the functional health of the early auditory system, including how speech is processed at different levels and how these levels interact. It will give clinicians a quantum leap in diagnostic power, enabling them to customize treatment and/or hearing device algorithms to a particular individual.

The synthetic sound-speech stimuli can provide a simultaneous assessment of multiple levels of the auditory system with realistic stimuli such as speech. Many different traditional techniques could be used to assess each level independently. However these methods generally: 1) would take too long to implement in the clinic and therefore would neither be adopted by clinicians nor reimbursed by insurers; 2) would lack the power to analyze relations among different levels of processing; and 3) do not even use actual speech or similar complex sounds, and therefore may not be representative of speech perception in everyday experience. One of the greatest challenges in the hearing loss industry is assessing how patients will perform in real environments, and to explain the variability among patients. This technology enables such an assessment.

The synthetic sound-speech stimuli can be adapted to different procedures through the selection of the elements and structure of the stimuli. Thus, the selection of the procedure can influence the selection of the characteristics of the elements.

In the typical case, the synthetic sound-speech stimuli will be created with speech stimuli that are frequency multiplexed with one or more sound stimuli. Any speech stimuli can be used, from brief isolated utterances to fully continuous running speech. In addition, one or more speech signals may be used simultaneously.

The speech stimuli are normally a common clinical speech corpus. A speech corpus is a database of speech audio files of specific utterances (e.g. words or sentences) that are naturally spoken by an actor. The speech corpus can also be custom tailored to a particular patient so that the speech corpus is a familiar voice, enabling the use of familiar voices in standard assessments, such as using a mother's own voice for infant screening.

The pitch of the speech corpus is preferably flattened to a constant value to ensure that the phase is consistent within the utterances. However, pitch flattening may be optional in some embodiments.

Next, a synthetic sound or sounds are selected. Typical sounds are chirps, clicks or brief noise bursts, with chirps being particularly preferred. The conventional click stimulus is a 100 μs pulse that has a frequency range from approximately 100 Hz to approximately 10,000 Hz. There are also many different types of chirps with a variety of characteristics that have been designed. These chirps have frequency components with timing that maximizes the response of the cochlea and increases the synchrony of neural firings of the auditory pathway.

The selected synthetic sound trains are spectrally multiplexed and temporally aligned with the modified speech corpus. That is, the frequency axis is split into alternating bands (e.g. approximately 0.5 to 1 octave wide) of speech and synthetic sound (e.g. chirp).

The frequency-multiplexed synthetic sound-speech stimulus can then be used in the context of the selected diagnostic system on a patient or test subject. In addition, libraries of frequency-multiplexed synthetic sound-speech stimuli can be developed that have stimuli with incremental variations in the sound and speech components.

There are many possible measurement or analysis techniques that can be adapted for use with the configurable synthetic sound-speech stimuli. For example, in one embodiment, the generated stimuli can be used to help determine the cause of hearing/language/selective attention impairment in an individual, and/or classification of individuals into sub-types of auditory processing disorders. A simple illustration is a "cortical hearing test" where the fidelity of speech processing by the higher brain is evaluated with the proposed stimulus, for instance in different EEG frequency ranges. Ultimately this would be compared to a normal hearing standard, as with typical clinical hearing tests. Such tests may incorporate traditional neural measures of auditory, linguistic and cognitive processing including but not limited to the mismatch negativity (MMN), N400, and P300. Such tests could also be used with varying pitch in non-tonal languages or in tonal languages (e.g. Mandarin) to assess the behavioral and/or brain response of 'tracking' changing pitch, whether it conveys linguistic or paralinguistic (e.g. prosodic) cues.

In another embodiment, the frequency-multiplexed synthetic sound-speech stimuli can be used to assess auditory function in a frequency-specific manner by using separate chirps limited to certain frequency bands rather than single chirps spanning the entire audible range.

The methods can be used to help audiologists fit hearing aids with greater accuracy, adaptively in real time, with lower return rates and increased customer satisfaction. The stimuli can be adapted to measure listening effort, which is a significant burden for the hearing impaired particularly in real-world acoustic situations. It can also be used to measure neural correlates of acceptable noise levels (ANL), currently one of the only reliable predictors of hearing aid use.

The methods can be used on a one-time or longitudinal basis with or without hearing impairment, e.g. for tracking degraded speech processing during normal aging, or for screening and early diagnosis of peripheral impairment and central auditory processing/language-based disorders in infants and children (e.g. wave V-SN10 or wave V-Vn deflection). The methods can be used in eliciting otoacoustic emissions (OAEs), e.g. in assessing auditory neuropathy.

The stimuli can also be used to enhance procedures that predict coma prognosis such as coma awakening by detecting auditory processing of pure tones or diagnose neuropsychiatric conditions characterized by altered auditory or linguistic function, such as schizophrenia.

The methods can be used in healthy or patient populations in brain-machine interfaces to provide feedback or to control a device, for instance changing settings for automatic speech recognition.

The stimuli characteristics can be altered in a controlled manner and used to assess specific component perceptual and neural processing abilities that comprise speech processing (for example fidelity of temporal processing wherein one may deliberately disrupt the chirp timing).

The stimuli and methods can be incorporated in broader behavioral and/or neural testing suites for perceptual and cognitive function (attention, working memory etc.). It can also be used to assess functional hemispheric laterality or asymmetry of auditory and cognitive processing.

The methods can be adapted for the use of music or any other complex sound containing transient events, whether periodic or non-periodic, where transient events could be frequency-multiplexed with a synthetic sound as described herein.

The stimuli can also be used with procedures to localize neural processing, either healthy or impaired, to specific anatomical structures, e.g. with EEG/MEG source localization techniques such as beam forming or through a combination with functional magnetic resonance imaging.

The multiplexing methods can also be used for processing sounds (with or without neural recording) such that they are heard better, more clearly or with greater comprehension by alternately multiplexing different sound streams to reduce acoustic masking. This could apply to the hearing impaired or to healthy listeners in acoustically adverse environments, e.g. public spaces, industry, or military (as in noisy land-based or air-based vehicles, or on the battlefield).

It is also possible to identify or "tag" one sound versus other sounds based on their neural processing, either primarily in response to the multiplexed synthetic sound or in combination with other acoustic attributes at multiple time scales. For instance two simultaneous talkers may be distinguished by different chirp rate (e.g. 38 Hz vs 43 Hz) and/or different speaking rate as reflected in the amplitude envelope, (e.g. 3 Hz vs 5 Hz).

The methods can also be adapted to be integrated into the function of portable and wearable consumer devices such as phones, tablets, watches, earphones, and headsets for processing audio signals (as in cellular/wireless voice communication) and for device command, control, and brain-device/device-brain feedback.

According to one aspect of the technology, an auditory stimulus is provided that has a speech component that is "frequency-multiplexed" with a synthetic sound that evokes strong early auditory system (including brainstem) responses, such as a chirp train.

A further aspect of the technology is to provide auditory stimuli that use synthetic sounds that are non-speech sounds selected from the group consisting of chirps, clicks, tones or tone-complexes, and amplitude-modulated noise bursts.

Another aspect of the technology is to provide a method for producing auditory stimuli where a speech component is frequency-multiplexed with a synthetic sound by splitting the frequency axis into alternating bands of speech and synthetic sound to minimize disruptive interaction between the speech and synthetic sounds along the basilar membrane and in their neural representations.

According to a further aspect of the technology, a method for analyzing electrical brain activity with frequency-multiplexed synthetic sound-speech stimuli is provided where the method is performed by executing programming on at least one computer processor with the programming residing on a non-transitory medium readable by the computer processor.

Further objects and aspects of the technology will be brought out in the following portions of the specification, wherein the detailed description is for the purpose of fully disclosing preferred embodiments of the technology without placing limitations thereon.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

The technology described herein will be more fully understood by reference to the following drawings which are for illustrative purposes only:

FIG. **1** is a schematic flow diagram of a method for producing frequency-multiplexed synthetic sound-speech stimuli for analyzing electrical brain activity according to one embodiment of the technology.

FIG. **2** is a time waveform and spectrogram (time-frequency plot) of a single chip according to an embodiment of the technology.

FIG. **3** shows how speech is frequency-multiplexed with chirp trains aligned to voicing according to an embodiment of the technology.

FIG. **4** shows chirps aligned in time with glottal pulses acceding to an embodiment of the technology.

FIG. **5** is a graph showing auditory brainstem response (ABR).

FIG. **6** is a graph that shows an auditory steady state response (ASSR) at 41 Hz.

FIG. **7** is a graph that shows a middle-latency response (MLR).

FIG. **8** is a graph that shows a long-latency response (LLR).

FIG. **9** is a graph that shows alpha power at 12 Hz over the parietal lobe.

FIG. **10** is a graph that shows ASSRs from an ancillary demonstration where two independent chirp-speech signals were presented dichotically (simultaneously with different signal in each ear).

DETAILED DESCRIPTION

Referring more specifically to the drawings, for illustrative purposes, embodiments of the apparatus and methods for frequency-multiplexed synthetic sound-speech stimuli and analyzing electrical brain activity are generally shown. Several embodiments of the technology are described generally in FIG. **1** through FIG. **10** to illustrate the methods. It will be appreciated that the methods may vary as to the specific steps and sequence and the apparatus may vary as to structural details without departing from the basic concepts as disclosed herein. The method steps are merely exemplary of the order that these steps may occur. The steps may occur in any order that is desired, such that it still performs the goals of the claimed technology.

Referring now to FIG. **1**, a method **10** for producing and using frequency-multiplexed synthetic sound-speech stimuli is depicted schematically. At block **12** of FIG. **1**, the test system that will utilize the synthetic sound-speech stimuli is selected. The characteristics of the stimuli that can be produced with the methods can be optimized and adapted to be used with both traditional and advanced techniques to analyze electrical brain activity. The nature of the detection apparatus and manner in which the electrophysiological signals that occur in response to the stimuli are detected may influence the configuration of the synthetic sound-speech stimuli that is developed.

Once the test system, stimuli and response detection system are selected, the synthetic sound-speech stimuli configuration can be determined. Table 1 provides a sample of frequency-multiplexed synthetic sound-speech stimuli generating MATLAB and Praat Code for generating stimuli according to one embodiment of the technology described herein.

At block **14** of FIG. **1**, at least one speech corpus is provided. A speech corpus is a database of speech audio files, usually read by an actor with text transcriptions, or may be composed of spontaneous speech or narratives. The speech can be produced by a live speaker or it can be synthesized, for example with text-to-speech algorithms. Any speech stimuli can be used at block **14**, from brief isolated utterances to fully continuous running speech. For instance, the method could be used on all common clinical speech corpuses such as HINT, QuickSIN or Synthetic Sentence Identification test. Speech stimuli based on the Harvard/IEEE (1969) speech corpus, a large set of low-context sentences that are thoroughly normed and widely used, are particularly suitable. In addition, one or more speech signals may be used simultaneously. The method can also be used in real time on streaming media or offline, after sounds are recorded.

At block **16** of FIG. **1**, the pitch of the sentences that are naturally spoken by an actor of the speech corpus is optionally flattened to a constant value or level. In one embodiment, the pitch constant is approximately 82 Hz, which is approximately the low limit of a male voice. However any value in the natural range of human pitch perception is acceptable.

The pitch is also flattened to a constant to ensure that voicing (glottal pulse) phase is consistent within utterances. This pitch flattening, a corollary to the primary technology of frequency-multiplexing, is not absolutely required but makes subsequent analysis more straightforward and robust. In one embodiment, the times of pitch-flattened glottal pulses are shifted by up to half a pitch period (+/−6 ms for a pitch of 82 Hz), to keep voicing phase consistent within and across speech utterances.

A synthetic sound or sounds that preferably evoke strong early auditory system (including brainstem) responses, such as a chirp train are then selected at block **18** of FIG. **1**. A standard chirp can be selected at block **18**, or the chirp can be customized to the individual listener. The sound intensity and other characteristics of the chirp can also be customized.

Other non-speech sounds such as clicks, tones or tone-complexes, or amplitude-modulated noise bursts could be used in the alternative, but chirps have been shown to be optimal and are particularly preferred. Additionally, if the pitch were not flattened, the chirps would not be isochronous and would track the changing pitch instead.

In Example 1, the chirp train that was selected was an isochronous 41 Hz series of "cochlear chirps." These chirps compensate for the traveling wave velocity in the basilar membrane, resulting in a more synchronized neural response and larger auditory brainstem response (ABR) as well as a potentially more robust middle latency responses (MLR) and long latency responses (LLR).

The selected train of synthetic sounds is frequency-multiplexed with the modified speech corpus at block **20** of FIG. **1** to produce synthetic sound-speech stimuli with characteristics determined in part by the speech and synthetic sound components and the configuration of the combination.

In one embodiment, the multiplexing at block **20** includes temporally aligning the synthetic sound trains with the modified speech. The frequency axis is split into alternating bands of speech and synthetic sound (chirps) to minimize disruptive interaction between the two sounds along the basilar membrane and in their neural representations, while ensuring that i) enough speech signal remains across all frequencies to be potentially intelligible, and ii) the speech perceptually blends with and is not perceptually masked by the synthetic sounds. The number of bands, width of bands, and relative intensity between speech and synthetic sound (chirp) may be adjusted to suit different purposes. The bands may be stable for a given sound or may vary over time, for instance to track the spectral peaks of formants. That is, the frequency bands that are multiplexed between speech and synthetic sound may be dynamic rather than stable over time. For instance, the spectral centers and widths of formant peaks during voiced epochs could define the centers and widths of the multiplexed chirp frequency bands, whereas speech energy would occupy all other bands (and all frequencies during unvoiced epochs).

In Example 1, these chirp trains only occur during voiced epochs of speech, and are temporally aligned with every other glottal pulse (except for near voicing onset, where the second chirp is omitted to allow cleaner assessment of an ABR and especially MLR). This alignment of the synthetic energy with glottal pulse energy, a corollary to the primary technology of frequency-multiplexing, helps the composite sound to blend into a single auditory object—an important attribute for higher level perception and cognition. Following the same principle, synthetic sounds can be temporally aligned with acoustic speech attributes in addition to glottal pulses, such as consonant plosives. Depending on the acoustics of the speech elements that are co-temporal with the synthetic sound, different synthetic sounds may be used at different moments, for example chirps during glottal pulses and noise bursts during plosives. The chirp-speech stimuli may therefore sound somewhat harsh or robotic but are largely natural and readily intelligible.

At block **22** of FIG. **1**, the synthetic sound-speech stimuli that are produced at block **20** can be incorporated into the test system that was selected at block **12**. It can be seen that the synthetic sound-speech stimuli that are produced can be used immediately on a test subject or they can be recorded and saved in a library of stimuli. The searchable library can include groups of synthetic sound-speech stimuli that have incremental variations in the characteristics of the components and multiplexed structure. Physiological responses to different synthetic sound-speech stimuli can also be compared and analyzed. A searchable library of a wide variety of different synthetic sound-speech stimuli combinations at block **22** will give the system greater sensitivity and accuracy.

Typically, the synthetic sound-speech stimulus is presented to at least one outer ear of a subject. However, the stimulus could be presented to both ears, with the same or different speech signal in each ear. For frequency-specific assessment of auditory function, the chirps could be presented not as single chirps that span multiple audible frequency bands, but as separate chirp segments occupying only certain frequency bands. Subjects need not perform a task. For example the subjects can either listen attentively to the speech stimulus or can watch a silent movie to maintain general arousal instead.

Furthermore, the generated stimulus need not be delivered acoustically, but could also apply to electrical transmission of speech signals, as with cochlear implants (CI). Minor differences would apply since there is no basilar membrane traveling wave delay in a cochlear implant. However the frequency-multiplexing of clicks or implant-electrode-multiplexing or other synthetic signals with speech would be useful in analogous ways to those described herein.

Cochlear implants add an additional means of recording early auditory potentials via the device itself, known generally as telemetry or telemetry-evoked compound action potential recording (of the auditory nerve), e.g. Advanced Bionics' Neural Response Imaging. The methods can also be used with CI telemetry to improve fitting and sound perception, upon implantation and over time, in analogous ways to those described for hearing aids.

While the primary technological advancement described herein includes methods for creating speech stimuli, their utility comes through analyzing neural responses to the stimuli with measuring and recording techniques including electroencephalography EEG, magnetoencephalography MEG, electrocorticography ECoG, and cochlear implant telemetry. For instance, EEG can be recorded with typical clinical systems, i.e. a small number of electrodes (e.g. 1-6, including one near vertex) with sampling rate high enough to capture the ABR (e.g. 16 kHz).

There are many possible measurement or analysis techniques that can be adapted for use with the configurable synthetic sound-speech stimuli. To illustrate the variety of applications of the configurable synthetic sound-speech stimuli, several conventional assessment procedures were adapted for use with synthetic sound-speech stimuli.

The following synthetic sound-speech stimuli methods can be illustrated in the following examples:

(1) Auditory brainstem response (ABR) following the presentation of chirp synthetic sounds. The ABR assesses neural responses from the auditory nerve through the inferior colliculus (IC), the most important integrative structure in the ascending auditory system. For instance wave V (or the V-Vn complex), the largest component, arises from the input to IC and its further processing, and therefore yields the single best measure of "bottom-up" auditory processing—how well sounds have been encoded into brain signals in the first place.

(2) MLR and Auditory steady state response (ASSR) at approximately 40 Hz. The ASSR shares generators with the middle latency response, and therefore characterizes sensory representations from thalamus to early, likely-primary auditory cortex—how well speech information is passed from lower to higher levels in the auditory system.

(3) Long-latency responses (LLRs) such as **P1/N1/P2** waves and the Temporal Response Function (TRF) for the speech envelope. The TRF is a linear kernel derived by reverse correlation between the low frequency (<40 Hz, e.g. 1-8 Hz) EEG/MEG and the speech amplitude envelope. LLRs measure the strength of speech representation in non-primary auditory cortex—how well speech information is represented in the higher auditory brain. Note the presence of synthetic sound trains (chirps), being co-temporal with epochs of high speech power (voicing), may yield more robust LLRs than speech alone.

(4) Alpha (8 Hz-12 Hz) power and laterality, over the occipitoparietal scalp, e.g. as an indicator of selective attention. This is a prime example of how the stimulus can be used in conjunction with high-level perceptual and cognitive measures.

In addition to these basic time or frequency measures, one can analyze time-frequency measures such as event-related spectral perturbation (ERSP, e.g. as implemented in EEGLAB), or trial-to-trial phase consistency. One can also analyze relationships among levels, from simple correlations between levels across time blocks (e.g. single-trial or 1 min running average of ABR wave V, ASSR power, and TRF amplitude) to more sophisticated cross-frequency, cross-time, and/or cross-location coupling. For instance, functional coupling of activity among different cortical brain areas has been shown to index numerous perceptual and cognitive functions. The present technology enables, for the first time, a vast array of functional measures to span the ascending auditory system as well. The mathematical or computational techniques to assess functional connectivity are numerous and include but are not limited to correlation/covariance and coherence-based methods, autoregressive-based methods (Granger causality), dynamic causal models, and analyses of network topology. Such methods can be applied in the time, spatial, and frequency domains (e.g. Partial Directed Coherence). Different states of speech processing or of functional connectivity can also be identified and classified with machine learning approaches to neural response patterns and data mining algorithms (e.g. blind source separation methods such as Independent Component Analysis).

The technology described herein may be better understood with reference to the accompanying examples, which are intended for purposes of illustration only and should not be construed as in any sense limiting the scope of the technology described herein as defined in the claims appended hereto.

Example 1

In order to demonstrate the technology, a "Functionally Integrated Speech Hierarchy" (FISH) assessment comprising a new speech stimulus corpus and advanced EEG analysis procedures was performed. For this illustration, 16 subjects with normal hearing and one subject with impaired hearing were recruited. EEG was acquired at 16 kHz with 20 channels distributed across the scalp while subjects listened attentively or watched a silent movie.

Sound attributes and analyses were jointly designed on mathematical and physiological principles to provide simultaneous but independent characterization of different levels of the ascending auditory system. The FISH assessment included multiple simultaneous measurements of the following:

1) Auditory brainstem response (ABR) to the first, last, and/or all chirps in each train. The ABR assesses neural responses from the auditory nerve through the inferior colliculus (IC), the most important integrative structure in the ascending auditory system. Wave V, the largest component, arises from the input to IC, and therefore gives the single best measure of "bottom-up" auditory processing. See FIG. **5**.

2) Middle Latency Response (MLR) and Auditory Steady State Response (ASSR) at 41 Hz. The ASSR shares generators with the middle latency response, and therefore characterizes sensory representations from thalamus to early, likely-primary auditory cortex.

3) Temporal Response Function (TRF) for the speech envelope. The TRF is a linear kernel derived by reverse correlation between the low frequency (<40 Hz) EEG and the speech envelope. LLR's measure the strength of speech representation in non-primary auditory cortex.

4) Alpha (8 Hz-12 Hz) power and laterality, over the occipito-parietal scalp, e.g. as an indicator of selective attention.

In addition to these basic measures, relationships among levels were analyzed, from simple correlations between levels across time blocks (e.g. 5 min running average of ABR wave V, ASSR power, and TRF amplitude) to more sophisticated cross-frequency, cross-time, and/or cross-location coupling.

A frequency-multiplexed chirp-speech stimulus was generated for the FISH assessment. The stimuli were based on the Harvard/IEEE (1969) speech corpus, a large set of low-context sentences that are widely used. The sentences were naturally spoken by an actor and the pitch was then flattened to a constant 82 Hz (the approximate lower limit of a male voice) and the glottal pulses were shifted (by +/−6 ms) to keep voicing phase consistent within utterances. FIG. **2** depicts a time waveform and spectrogram (time-frequency plot) of a single chirp that was part of the chirp train.

Next, the speech was "spectrally multiplexed" with a chirp train. That is, the frequency axis was split into alternating bands approximately 1 octave wide of speech and chirps in this illustration. The chirp train was an isochronous series of 41 Hz "cochlear chirps," which compensate for the traveling wave velocity in the basilar membrane, resulting in a more synchronized neural response and larger auditory brainstem response (ABR). FIG. **3** illustrates how speech is frequency-multiplexed with chirp trains that are aligned to voicing. These trains only occur during voiced epochs of speech and are temporally aligned with every other glottal pulse (except for near voicing onset, where the second chirp is dropped to allow cleaner assessment of an ABR and MLR). FIG. **4** shows chirps aligned in time with glottal pulses. The FISH speech stimuli therefore sound somewhat harsh or robotic but were found to be largely natural and readily intelligible.

Example 2

To further demonstrate the technology, neural responses to the same frequency-multiplexed chirp-speech stimuli were performed from a group of 17 subjects. In this example, the chirp train component was an isochronous 41 Hz series of "cochlear chirps". These chirps compensate for the traveling wave velocity in the basilar membrane, resulting in a more synchronized neural response and larger auditory brainstem response (ABR) as well as a potentially more robust middle latency responses (MLR) and long latency responses (LLR).

FIG. **5** is a graph showing auditory brainstem response (ABR) of a test subject that was presented the frequency-multiplexed chirp-speech stimulus of Example 1. FIG. **6** is a graph of the auditory steady state response (ASSR). FIG. **7** shows middle-latency response (MLR) and FIG. **8** shows the long-latency response (LLR). FIG. **9** shows alpha power at 12 Hz over the parietal lobe, demonstrating how the stimulus can be used in conjunction with high-level perceptual and cognitive measures.

Example 3

Auditory Steady State Response (ASSR) responses for simultaneous chirp-speech stimulus signals were taken to characterize how well speech information is passed from lower to higher levels in the auditory system. FIG. **10** shows ASSRs from an ancillary demonstration where two independent chirp-speech signals were presented dichotically (simultaneously with different signal in each ear). In this case the pitches and therefore chirp rates were different between ears: 38 Hz and 43 Hz. Chirps and speech were frequency-multiplexed in opposing bands between the ears, such that a given band contained chirps for one ear and speech for the other.

From the discussion above it will be appreciated that the technology described herein can be embodied in various ways, including the following:

1. A method for generating synthetic sound-speech stimuli for analyzing electrical brain activity, the method comprising: (a) providing at least one speech corpus having a plurality of utterances; (b) selecting a train of synthetic sounds; and (c) multiplexing the train of synthetic sounds with the speech corpus; (d) wherein the synthetic sounds are temporally aligned with the utterances of the speech corpus.

2. The method of any preceding embodiment, further comprising: flattening speech corpus pitch to an approximately constant value; and temporally shifting glottal pulses of the speech corpus; wherein voicing phase is kept consistent within and across speech utterances.

3. The method of any preceding embodiment, wherein the pitch constant value is approximately 82 Hz, the lower limit of a male voice.

4. The method of any preceding embodiment, wherein times of pitch-flattened glottal pulses are shifted by approximately half a pitch period or less.

5. The method of any preceding embodiment, wherein the speech corpus is a common clinical speech corpus selected from the group consisting of HINT, QuickSIN, Synthetic Sentence Identification test and the Harvard/IEEE (1969) speech corpus.

6. The method of any preceding embodiment, wherein the synthetic sound is a non-speech sound selected from the group consisting of chirps, clicks, tones, tone-complexes, and amplitude-modulated noise bursts.

7. The method of any preceding embodiment, wherein the synthetic sound is an isochronous or non-isochronous chirp train.

8. The method of any preceding embodiment, wherein the synthetic sound is an isochronous 41 Hz series of cochlear chirps.

9. The method of any preceding embodiment claim **1**, wherein the frequency multiplexing further comprises: splitting a frequency axis into alternating bands of speech and synthetic sound; wherein disruptive interactions between the speech and synthetic sounds along the basilar membrane and in their neural representations are minimized.

10. The method of any preceding embodiment, further comprising: temporally aligning the synthetic sounds to consonant plosives and glottal pulses of the speech corpus.

11. A method for analyzing electrical brain activity from auditory stimuli, the method comprising: (a) providing one or more frequency-multiplexed synthetic sound-speech stimuli; (b) presenting at least one stimulus to a test subject; and (c) evaluating detected electrophysiological responses of the test subject to the applied stimulus.

12. The method of any preceding embodiment, further comprising: incorporating the frequency-multiplexed synthetic sound-speech stimuli in a neural or behavioral test system that utilizes an auditory stimuli.

13. The method of any preceding embodiment, wherein the test system is a test selected from the group of tests consisting of the Auditory Brainstem Response (ABR), Middle Latency Response (MLR), Auditory Steady State Response (ASSR), and Long Latency Response (LLR).

14. The method of any preceding embodiment, wherein the frequency-multiplexed synthetic sound-speech stimuli is provided from a library of stimuli.

15. The method of any preceding embodiment, wherein the frequency-multiplexed synthetic sound-speech stimuli is generated with the steps comprising: providing at least one speech corpus having a plurality of utterances; selecting a train of synthetic sounds; and multiplexing the train of synthetic sounds with the speech corpus to produce the stimuli; wherein the synthetic sounds are temporally aligned with the utterances of the speech corpus.

16. The method of any preceding embodiment, further comprising: flattening speech corpus pitch to an approximately constant value; and temporally shifting glottal pulses of the speech corpus; wherein voicing phase is kept consistent within and across speech utterances.

17. The method of any preceding embodiment, wherein the speech corpus is a common clinical speech corpus selected from the group consisting of HINT, QuickSIN, Synthetic Sentence Identification test and the Harvard/IEEE (1969) speech corpus.

18. The method of any preceding embodiment, wherein the synthetic sound is a non-speech sound selected from the group consisting of chirps, clicks, tones, tone-complexes, and amplitude-modulated noise bursts.

19. The method of any preceding embodiment, wherein the frequency multiplexing further comprises: splitting a frequency axis into alternating bands of speech and synthetic sound; wherein disruptive interactions between the speech and synthetic sounds along the basilar membrane and in their neural representations are minimized.

20. The method of any preceding embodiment, further comprising: temporally aligning the synthetic sounds to consonant plosives and glottal pulses of the speech corpus.

21. A system for detecting and analyzing electrical brain activity, comprising: (a) at least one detector; (b) a computer processor; and (c) a non-transitory computer-readable memory storing instructions executable by the computer processor; (d) wherein the instructions, when executed by the computer processor, perform steps comprising: (i) providing at least one speech corpus having a plurality of utterances; (ii) flattening speech corpus pitch to an approximately constant value; (iii) temporally shifting glottal pulses of the speech corpus; (iv) providing a train of synthetic sounds that evoke strong auditory system responses; (v) multiplexing the train of synthetic sounds with the speech corpus so that the synthetic sounds are temporally aligned with the utterances of the speech corpus to produce the stimuli; and (vi) detecting electrophysiological responses of a test subject to the applied stimulus with the detector.

22. The system of any preceding embodiment, wherein the detector is selected from the group of detectors consisting of electroencephalography EEG, magnetoencephalography MEG, electrocorticography ECoG, and cochlear implant telemetry.

23. The system of any preceding embodiment, wherein the speech corpus is a common clinical speech corpus selected from the group consisting of HINT, QuickSIN, Synthetic Sentence Identification test and the Harvard/IEEE (1969) speech corpus.

24. The system of any preceding embodiment, wherein the synthetic sound is a non-speech sound selected from the group consisting of chirps, clicks, tones, tone-complexes, and amplitude-modulated noise bursts.

25. The system of any preceding embodiment, the instructions further comprising: temporally aligning the synthetic sounds to consonant plosives and glottal pulses of the speech corpus.

Embodiments of the present technology may be described with reference to flowchart illustrations of methods and systems, and/or algorithms, formulae, or other computational depictions, which may also be implemented as computer program products. In this regard, each block or step of a flowchart, and combinations of blocks (and/or steps) in a flowchart, algorithm, formula, or computational depiction can be implemented by various means, such as hardware, firmware, and/or software including one or more computer program instructions embodied in computer-readable program code logic. As will be appreciated, any such computer program instructions may be loaded onto a computer, including without limitation a general purpose computer or special purpose computer, or other programmable processing apparatus to produce a machine, such that the computer program instructions which execute on the computer or other programmable processing apparatus create means for implementing the functions specified in the block(s) of the flowchart(s).

Accordingly, blocks of the flowcharts, algorithms, formulae, or computational depictions support combinations of means for performing the specified functions, combinations of steps for performing the specified functions, and computer program instructions, such as embodied in computer-readable program code logic means, for performing the specified functions. It will also be understood that each block of the flowchart illustrations, algorithms, formulae, or computational depictions and combinations thereof described herein, can be implemented by special purpose hardware-based computer systems which perform the specified functions or steps, or combinations of special purpose hardware and computer-readable program code logic means.

Furthermore, these computer program instructions, such as embodied in computer-readable program code logic, may also be stored in a computer-readable memory that can direct a computer or other programmable processing apparatus to function in a particular manner, such that the instructions stored in the computer-readable memory produce an article of manufacture including instruction means which implement the function specified in the block(s) of the flowchart(s). The computer program instructions may also be loaded onto a computer or other programmable processing apparatus to cause a series of operational steps to be performed on the computer or other programmable processing apparatus to produce a computer-implemented process such that the instructions which execute on the computer or other programmable processing apparatus provide steps for implementing the functions specified in the block(s) of the flowchart(s), algorithm(s), formula(e), or computational depiction(s).

It will further be appreciated that the terms "programming" or "program executable" as used herein refer to one or more instructions that can be executed by a processor to perform a function as described herein. The instructions can be embodied in software, in firmware, or in a combination of software and firmware. The instructions can be stored local to the device in non-transitory media, or can be stored remotely such as on a server, or all or a portion of the instructions can be stored locally and remotely. Instructions stored remotely can be downloaded (pushed) to the device by user initiation, or automatically based on one or more factors. It will further be appreciated that as used herein, that the terms processor, computer processor, central processing unit (CPU), and computer are used synonymously to denote a device capable of executing the instructions and communicating with input/output interfaces and/or peripheral devices.

Although the description herein contains many details, these should not be construed as limiting the scope of the disclosure but as merely providing illustrations of some of the presently preferred embodiments. Therefore, it will be appreciated that the scope of the disclosure fully encompasses other embodiments which may become obvious to those skilled in the art.

In the claims, reference to an element in the singular is not intended to mean "one and only one" unless explicitly so stated, but rather "one or more." All structural, chemical, and functional equivalents to the elements of the disclosed embodiments that are known to those of ordinary skill in the art are expressly incorporated herein by reference and are intended to be encompassed by the present claims. Furthermore, no element, component, or method step in the present disclosure is intended to be dedicated to the public regardless of whether the element, component, or method step is explicitly recited in the claims. No claim element herein is to be construed as a "means plus function" element unless the element is expressly recited using the phrase "means for". No claim element herein is to be construed as a "step plus function" element unless the element is expressly recited using the phrase "step for".

TABLE 1

```
% CHEECH_STIMGEN.M (MATLAB function)
function [signal,cuelat,cuelabl]=cheech_stimgen(outputPath,f0,filterSpeechBands,
filterChirpBands,stimcue,cueplus,invert)
% CHEECH_STIMGEN.M
% Function to generate chirp-speech multiplexed stimulus designed to evoke
% neural activity from various processing levels along the ascending
% human auditory pathway, including the Auditory Brainstem
% Response (ABR), Middle Latency Response (MLR), Auditory Steady State
% Response (ASSR), and Long Latency Response (LLR).
% Inputs:
%                   outputPath = output path, with trailing slash;
%                   f0 = fundamental for checking voicing phase. This MUST be
%                               confirmed same as what is hardcoded in
%                               FlatIntonationSynthesizer.psc. Default =82;
%                   filterSpeechBands = [250 500; 1000 2000; 4000 0]; % set
%                            speech filter STOP bands;use '0' for low or high-pass
%                   filterChirpBands = [0 250; 500 1000; 2000 4000]; % chirp
%                               filter STOP bands; use '0' for low or high-pass
%                   stimcue = code used as wav cue at stim onset; default = 10, to %
%                         indicate e.g. stimulus or experimental conditions in %
%                      the eeg file
%                   cueplus = 0; %additive index for disambiguating wave cues, as
%                                  when cue numbering different for right vs left
%                                  ear; e.g. 0 for left ear(cues 99, 100, etc);
%                                  100 for right ear (cues 199, 200, etc).
%                   invert = 0; %flag to invert entire waveform before writing.
%                                  0 = no (default) or 1 = yes
%
% This function makes use of several additional resources:
% -The Harvard/IEEE (1969)speech corpus, spoken by a male actor
% -The PRAAT acoustic analysis software package (www.praat.org)
% -Chirp auditory stimuli from Elberling, Callo, & Don 2010, part of the
%   Auditory Modelling Toolbox (http://amtoolbox.sourceforge.net/doc/)
% - filters from the ERPlab toolbox ca. 2013 (filterb.m, filter_tf.m)
%                      (http://erpinfo.org/erplab); IIR Butterworth zero phase
%                      using matlab's filtfilt.m
%% defaults
if ~exist('stimcue','var')
    stimcue = 10;
end
if ~exist('cueplus','var')
    cueplus = 0;
end
if ~exist('invert','var')
    invert = 0;
end
catNum = 50; % specify number of sentences to concatenate
gmin=0.050; % minimum leading &/or trailing silence between sentences when
            concatenated, in sec
thr = 0.01; % speech envelope threshold, used for identifying and
            demarcating silences
```

TABLE 1-continued

```
voiceFilt = [20 1000]; % in Hz. bandpass filter to create envelope used for
            identifying voicing by power (and avoid fricatives)
voiceThresh = 0.015% threshold to identify voiced periods (from power in
            lowpass filtered speech)
minimumChirpCycles = 4; % minimum voiced duration in order to add chirps
ampchirp = 0.15% normalized chirp amplitude to match speech power in corpus
plotflag=0;
  %% First Concatenate sentences (these recordings are at 22050 Hz sampling
rate)
corpusPath= ‘C:\IEEE_male\’;
fileList = dir([corpusPath ‘*.wav’]); % get a list of files
for stim=1:1 % (loop in case you wish to batch process many stimuli)
    signal = [ ];
    for sentNum = 1:catNum
        fileName = [corpusPath fileList(sentNum+((stim+−1)*catNum)).name];
        [trimSentence,Fs,gap] = silence_trim(fileName,thr,gmin,plotflag);
        signal=[signal ; trimSentence]; % Concatenate trimmed sentences
    end
    wavwrite(signal,Fs,[ outputPath ‘stim’ num2str(stim) ‘.wav’]);
    disp( [ outputPath ‘stim’ num2str(stim) ‘.wav’] )
end
%% Now ‘flatten’ speech pitch with PRAAT
% wav files must be in outputPath
% FILES WILL BE OVERWRITTEN WITH FLATTENED VERSIONS
% both pratcon.exe and the FlatIntonationSynthesizer.psc script must be
% at this location
cd(outputPath);
% now call PRAATCON, which will synthesize glottal pulses at the frequency
% specified in FlatIntonationSynthesizer.psc (currently 82Hz)
disp(‘Note, the Praat flattening script overwrites the originals; also it is currently
hardcoded for frequency - check that you have the right one’);
[status,result]=system([outputPath ‘praatcon FlatIntonationSynthesizer.psc’])
fo stimNum = 1:1   % loop for batching many stims
% Process the speech signal
flatSpeechUnfiltered = [‘stim’ num2str(stimNum) ‘.wav’];
[flatSpeech,Fs,Nbits]=wavread(flatSpeechUnfiltered);
disp(‘Lowpass filtering to identify voiced periods by their power (and avoid
fricatives).’)
flatSpeechlow = filterb(flatSpeech,[0 voiceFilt(1); voiceFilt(2) 0], Fs, 10);
y = abs(hilbert(flatSpeechlow));
tempenv = filterb(y,[0 0.0001; 40 0], Fs, 4);
figure, plot(tempenv), title(‘tempenv’)
% identify phase of synthesized glottal pulses so chirps can be aligned
[phaseoff,timeoff,envoice,envhist] = voicing_phase(flatSpeech,Fs,f0,plotflag);
sampleoff = round( Fs * timeoff) ; % phase offset in samples method 2
% filter the flattened speech
filterorder = 20;
flatSpeech = filterb(flatSpeech,filterSpeechBands, Fs, filterorder); % filter
  %% generate the chirp Train
chirpFreq = f0/2; % in Hz; in this case half the voiced fundamental
chirpInterval=Fs/chirpFreq;
repeats = ceil(length(flatSpeech) / chirpInterval ); % Number of chirps per burst
constantOffset = 0; % this value is used to precisely align every chirp to the
speech glottal pulses
chirpPath = ‘C:\chirps\’;
chirpLength = 343; % in this case actual chirp waveforms are just first 343
samples (16ms @ 22050Hz)
[chirp1,FsChirp,nBits] = wavread([chirpPath ‘chirp1_22kHz.wav’]); % sample is
30ms long at 22050 kHz.
if Fs~=FsChirp
    error(‘Sampling rate of sounds and chirp wav are different’)
end
chirp1 = chirp1(1:chirpLength);
chirpIndices = round (((0:repeats)*chirpInterval) + 1 );
chirpTrain = zeros(chirpIndices(end),1);
for chirpNum = 2:repeats+1
    chirpTrain(chirpIndices(chirpNum)−(chirpLength−1):chirpIndices(chirpNum)) =
chirp1;
end
leadingSilence = 0.005; % in seconds; this is just to give some onset time so
                                          % EEG acquisition software doesn’t miss the first cue
leadingSilence = zeros(Fs*leadingSilence,1); % in samples
% Shift the chirp train to align with glottal pulses
chirpTrain = [leadingSilence; zeros(sampleoff + constantOffset ,1); chirpTrain];
chirpIndices = chirpIndices + length(leadingSilence) + sampleoff + constantOffset;
chirpTrain=ampchirp .* chirpTrain(1:length(flatSpeech)); % set the
%                                 chirpTrain amplitude and shorten length to match voice sample
%                                 also shift speech signal to play nice with EEG acquisition
flatSpeech = [ leadingSilence ; flatSpeech];
```

TABLE 1-continued

```
% filter the chirp train:
filterorder = 20;
chirpTrain = filterb(chirpTrain,filterChirpBands, Fs, filterorder);
chirpTrainForVoice = zeros(length(flatSpeech),1);   % generate a blank chirp
                                                         % train for later
%% now insert full chirps only during voiced segments
V=tempenv;
V(V<=voiceThresh) = 0; V(V>0) = 1;
D = diff([0,V',0]);                              %find onsets and offsets of voiced segments
voiceStart = find(D == 1);
voiceStop = find(D == -1) - 1;
figure; hold on
plot(tempenv,'k');plot(flatSpeech)
cuelat = [ ]; cuelat(1) = 0;                     % needed for writing the trigger cues into
                                                      % wav files, to indicate chirp times to eeg
                                                      % acquisition software
cuelabl = [ ]; cuelabl{1} = num2str(stimcue);
for voicedSegment=1:length(voiceStart)
            chirpIndicesForVoice = find(chirpIndices > voiceStart(voicedSegment) &
                            chirpIndices < voiceStop(voicedSegment) );
    if length(chirpIndicesForVoice) > minimumChirpCycles &&
            ~isempty(chirpIndicesForVoice)
            chirpTrainForVoice( chirpIndices(chirpIndicesForVoice(1)-
                            1):chirpIndices(chirpIndicesForVoice(1)) )= ...
            chirpTrain(chirpIndices(chirpIndicesForVoice(1)-
                            1):chirpIndices(chirpIndicesForVoice(1)));
              % drop the second chirp in order to extract Middle Latency Response
              chirpTrainForVoice(chirpIndices(chirpIndicesForVoice(2)):
                            chirpIndices(chirpIndicesForVoice(end)) )= ...
                            chirpTrain(chirpIndices(chirpIndicesForVoice(2)):
                            chirpIndices(chirpIndicesForVoice(end)));
        cueNum = 1;
        cuelat(end+1)= chirpIndices(chirpIndicesForVoice(cueNum));
                                                 % in samples
        cuelabl{end+1}= num2str( (cueNum-1) + 100 + cueplus);
                                                 % cue label (text string)
        % (drop the second chirp in order to extract Middle Latency Response)
        for cueNum = 3:length(chirpIndicesForVoice)
            cuelat(end+1)= chirpIndices(chirpIndicesForVoice(cueNum));
                                                 % in samples
            cuelabl{end+1}= num2str( (cueNum-1) + 100 + cueplus);
                                                 % cue label (text string)
        end
              % give last chirp in voiced epoch special label
        cuelabl{end}= num2str(99 + cueplus) ; % cue label (text string)
    end
    end
%% check range of the trigger cues
if max(cellfun(@str2num, cuelabl))>255 | min(cellfun(@str2num, cuelabl))<0
    warning('you have wav cues outside the range [0,255]! These may not work
            to send parallel port triggers')
end
% combine (MULTIPLEXED) speech and chirps
signal = flatSpeech+chirpTrainForVoice;
% phase invert if desired
if invert
    signal = -signal;
end
% and convert multiplexed stimulus to mono or stereo
channels = 0; % 0=mono, 1=left, 2=right, 3=binaural
switch channels
    case 0 % mono
        %(do nothing)
    case 1 % left chan
        signal = [signal zeros(length(signal),1)];
    case 2 % right chan
        signal = [zeros(length(signal),1) signal];
    case 3 % both chans
        signal = [signal signal];
end
   % finally, write the sound file and add trigger event cues
wavwrite(signal,Fs,[outputPath flatSpeechUnfiltered(1:end-4)
                            'Multiplex.wav'])
            %must write the file first *before* adding trigger cues
addWavCue(outputPath,[flatSpeechUnfiltered(1:end-4)
            'Multiplex.wav'],cuelat,cuelabl,[flatSpeechUnfiltered(1:end-4)
            'MultiplexCUED.wav']) % adds cues info to a metadata block in wav file
end % stimNum
PRAAT FLAT INTONATION SYNTHESIZER
#
```

TABLE 1-continued

```
# Resynthesizes all the sound files in the
# specified directory to have flat pitch
# of the specified frequency. Files are
# saved in a specified directory.
#
##########################
sound_directory$ = “c:\temp\”
sound_file_extension$ = “.wav”
end_directory$ = “c:\temp\”
resynthesis_pitch = 82 #for our demonstration, 82Hz
# Here, you make a listing of all the sound files in a directory.
Create Strings as file list... list ‘sound_directory$’*‘sound_file_extension$’
numberOfFiles = Get number of strings
for ifile to numberOfFiles
filename$ = Get string... ifile
# A sound file is opened from the listing:
Read from file... ‘sound_directory$’‘filename$’
sound_one$ = selected$ (“Sound”)
To Manipulation... 0.01 60 400
# Create a new pitch tier with the flat pitch:
select Sound ‘sound_one$’
start = Get start time
end = Get end time
Create PitchTier... ‘sound_one$’ start end
Add point... start resynthesis_pitch
Add point... end resynthesis_pitch
# Combine and save the resulting file:
select Manipulation ‘sound_one$’
plus PitchTier ‘sound_one$’
Replace pitch tier
select Manipulation ‘sound_one$’
Get resynthesis (PSOLA)
Write to WAV file... ‘end_directory$’‘filename$’
select Sound ‘sound_one$’
plus Manipulation ‘sound_one$’
plus PitchTier ‘sound_one$’
Remove
select Strings list
endfor
select all
Remove
```

What is claimed is:

1. A method for analyzing electrical brain activity from auditory stimuli, the method comprising:

(a) providing one or more frequency-multiplexed synthetic sound-speech stimuli, wherein the stimuli comprise at least one speech corpus that is multiplexed with a train of synthetic sounds;

(b) presenting at least one stimulus from an audio system to a test subject;

(c) detecting an electrophysiological response from the test subject to the presented stimulus; and

(d) evaluating the detected electrophysiological response of the test subject.

2. The method as recited in claim **1**, further comprising: incorporating the frequency-multiplexed synthetic sound-speech stimuli in a neural or behavioral test system that utilizes auditory stimuli.

3. The method as recited in claim **2**, wherein said test system is a test selected from the group of tests consisting of the Auditory Brainstem Response (ABR), Middle Latency Response (MLR), Auditory Steady State Response (ASSR), and Long Latency Response (LLR).

4. The method as recited in claim **1**, wherein said one or more frequency-multiplexed synthetic sound-speech stimuli are provided from a library of stimuli.

5. The method as recited in claim **1**, wherein said one or more frequency-multiplexed synthetic sound-speech stimuli are generated with the steps comprising:

providing at least one speech corpus having a plurality of utterances;

selecting a train of synthetic sounds; and

multiplexing the train of synthetic sounds with the speech corpus to produce the stimuli;

wherein the synthetic sounds are temporally aligned with the utterances of the speech corpus.

6. The method as recited in claim **5**, further comprising:

flattening speech corpus pitch to an approximately constant value; and

temporally shifting glottal pulses of the speech corpus;

wherein voicing phase is kept consistent within and across speech utterances.

7. The method as recited in claim **6**, wherein the speech corpus pitch is flattened to a constant value of approximately 82 Hz, the lower limit of a male voice.

8. The method as recited in claim **6**, wherein times of pitch-flattened glottal pulses are shifted by approximately half a pitch period or less.

9. The method as recited in claim **5**, wherein the speech corpus is a common clinical speech corpus selected from the group consisting of HINT, QuickSIN, Synthetic Sentence Identification test and the Harvard/IEEE (1969) speech corpus.

10. The method as recited in claim **5**, wherein the synthetic sound is a non-speech sound selected from the group consisting of chirps, clicks, tones, tone-complexes, and amplitude-modulated noise bursts.

11. The method as recited in claim **5**, wherein the frequency multiplexing further comprises:

splitting a frequency axis into alternating bands of speech and synthetic sound;

wherein disruptive interactions between the speech and synthetic sounds along the basilar membrane and in their neural representations are minimized.

12. The method as recited in claim **5**, further comprising:

temporally aligning said synthetic sounds to consonant plosives and glottal pulses of the speech corpus.

13. The method as recited in claim **5**, wherein the synthetic sound is an isochronous or non-isochronous chirp train.

14. The method as recited in claim **5**, wherein the synthetic sound is an isochronous 41 Hz series of cochlear chirps.

15. A method for analyzing electrical brain activity from auditory stimuli, the method comprising:

(a) providing one or more frequency-multiplexed synthetic sound-speech stimuli, wherein the stimuli comprise at least one speech corpus that is multiplexed with a train of synthetic sounds such that the stimuli comprise a frequency axis split into two or more bands of speech and synthetic sound;

(b) presenting at least one stimulus from an audio system to a test subject;

(c) detecting an electrophysiological response of the test subject to the presented stimulus; and

(d) evaluating the detected electrophysiological response of the test subject.

16. The method as recited in claim **15**, wherein the speech corpus is a common clinical speech corpus selected from the group consisting of HINT, QuickSIN, Synthetic Sentence Identification test and the Harvard/IEEE (1969) speech corpus.

17. The method as recited in claim **15**, wherein the speech corpus is a speech utterance.

18. The method as recited in claim **15**, wherein the synthetic sound is a non-speech sound selected from the group consisting of chirps, clicks, tones, tone-complexes, and amplitude-modulated noise bursts.

19. The method as recited in claim **15**, wherein the synthetic sound is an isochronous or non-isochronous chirp train.

20. The method as recited in claim **15**, wherein said one or more frequency-multiplexed synthetic sound-speech stimuli are provided from a library of stimuli.

* * * * *

Cortical Tracking of Speech: Toward Collaboration between the Fields of Signal and Sentence Processing

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Abstract

■ In recent years, a growing number of studies have used cortical tracking methods to investigate auditory language processing. Although most studies that employ cortical tracking stem from the field of auditory signal processing, this approach should also be of interest to psycholinguistics—particularly the subfield of sentence processing—given its potential to provide insight into dynamic language comprehension processes. However, there has been limited collaboration between these fields, which we suggest is partly because of differences in theoretical background and methodological constraints, some mutually exclusive. In this paper, we first review the theories and methodological constraints that have historically been prioritized in each field and provide concrete examples of how some of these constraints may be reconciled. We then elaborate on how further collaboration between the two fields could be mutually beneficial. Specifically, we argue that the use of cortical tracking methods may help resolve long-standing debates in the field of sentence processing that commonly used behavioral and neural measures (e.g., ERPs) have failed to adjudicate. Similarly, signal processing researchers who use cortical tracking may be able to reduce noise in the neural data and broaden the impact of their results by controlling for linguistic features of their stimuli and by using simple comprehension tasks. Overall, we argue that a balance between the methodological constraints of the two fields will lead to an overall improved understanding of language processing as well as greater clarity on what mechanisms cortical tracking of speech reflects. Increased collaboration will help resolve debates in both fields and will lead to new and exciting avenues for research. ■

INTRODUCTION

Recent years have seen a growing interest in the cortical tracking of speech as a potential measure of acoustic, linguistic, and cognitive processing (Meyer, Sun, & Martin, 2020; Obleser & Kayser, 2019; Kösem & van Wassenhove, 2017; Meyer, 2018; see Tyler, 2020). The terms "cortical tracking" or "speech tracking" loosely refer to continuous neural activity that is somehow time-locked to ongoing events in the speech signal. According to one common interpretation, cortical tracking reflects the tendency for neural oscillations to align, or phase-lock, with quasiperiodic features in the speech signal. These quasiperiodic elements of speech can be acoustic, such as the fluctuations in the amplitude envelope associated with syllables (Doelling, Arnal, Ghitza, & Poeppel, 2014; Peelle, Gross, & Davis, 2013) or linguistic representations generated in the mind of the listener, such as syntactic phrase boundaries (Meyer, Henry, Gaston, Schmuck, & Friederici, 2017; Ding, Melloni, Zhang, Tian, & Poeppel, 2016). Researchers adopting this approach often refer to cortical tracking as "neural entrainment" (Obleser & Kayser, 2019; see later sections for further discussion of terminology and debates in this field). It has been proposed that entrainment may contribute to improved speech processing and language comprehension—for instance, by instantiating temporal predictions that enable segmentation of the continuous speech signal into units at several timescales (Keitel, Gross, & Kayser, 2018; Kösem et al., 2018; Meyer & Gumbert, 2018; Meyer et al., 2017; Ding et al., 2016; Zoefel & VanRullen, 2015; Doelling et al., 2014; Peelle et al., 2013; Giraud & Poeppel, 2012; Peelle & Davis, 2012; Ahissar et al., 2001).

Cortical tracking methods should therefore be of great interest to researchers studying sentence processing from a psycholinguistic perspective. Sentence processing research makes frequent use of ERPs to draw inferences about neural responses to isolated, discrete events such as word onsets or sentence boundaries (Swaab, Ledoux, Camblin, & Boudewyn, 2012; Kutas & Federmeier, 2011; Kutas, Van Petten, & Kluender, 2006) as well as time–frequency analyses of EEG oscillatory power at specific bands (Prystauka & Lewis, 2019). However, the field of sentence processing has yet to fully incorporate cortical tracking as a tool to investigate language processing mechanisms continuously, rather than at discrete epochs.

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Journal of Cognitive Neuroscience 33:4, pp. 574–593
https://doi.org/10.1162/jocn_a_01676

As we will argue, combining measures of cortical tracking with typical psycholinguistic paradigms may help resolve long-standing debates and distinguish between competing theories of language processing, while also making use of continuous EEG data that are typically treated as noise in ERP paradigms (a point we discuss further in the section titled Contributions to Psycholinguistics).

In general, there has been limited collaboration between signal processing neuroscientists who use cortical tracking paradigms and psycholinguists, despite the fact that both fields share the common goal of elucidating how listeners process spoken language. To be more specific, the research areas that are most relevant for our purposes are the study of human sentence processing, which is a subfield of psycholinguistics, and the study of auditory signal processing, which is often carried out by perceptual neurophysiologists and engineers who are interested in how the brain transforms auditory signals and who may implement cortical tracking in their research methods. These research topics intersect when the auditory signal comprises spoken sentences. For convenience, we will refer to these research areas as "sentence processing" and "signal processing" throughout, with the caveat that the fields are not mutually exclusive; there are psycholinguists who employ cortical tracking methods to study sentence processing (e.g., Song & Iverson, 2018; Martin & Doumas, 2017; Meyer et al., 2017), signal processing researchers who are interested in the linguistic properties of the speech signal (e.g., Ding et al., 2016), and investigators with clear interest in both fields who already conduct studies that incorporate the methodological compromises we suggest later on (e.g., Giraud & Poeppel, 2012; Peelle & Davis, 2012; Obleser & Kotz, 2011).

Despite these notable examples of interaction, the two fields remain largely independent. Part of the reason for this limited collaboration stems from the different ways these two fields conceptualize and define language processing; whereas sentence processing research focuses on the cognitive and linguistic representations formed during comprehension, signal processing research treats speech as an example of a complex auditory signal and seeks to characterize the system that transforms that input signal into an output signal or response (e.g., Rimmele, Morillon, Poeppel, & Arnal, 2018; Morillon & Schroeder, 2015). An additional hurdle to collaboration stems from the largely different methodological constraints that the two fields are primarily concerned with. Some of these constraints are because of the theoretical grounds upon which research is conducted as well as limitations in the current methods for data acquisition; these are sometimes at odds across fields and can be difficult to reconcile. However, we argue that most constraints are reconcilable and that both fields would benefit from incorporating aspects of each other's methodology and theoretical constructs. Just as sentence processing research would be able to answer more detailed questions about linguistic processing by using more of the continuous EEG data through cortical tracking methods, signal processing research would gain a better understanding of the role of cortical tracking in the processing of speech by controlling and manipulating the linguistic features of the stimulus, which are often underspecified in current studies.

In this paper, we first review the theoretical background and the methodological constraints that have historically been prioritized in the study of sentence processing and the neuroscience of auditory signal processing. We then explore in more detail what further collaboration between these two fields could bring, highlighting how cortical tracking methods could be used to improve our understanding of continuous sentence comprehension and how paradigms from psycholinguistics may in turn improve our understanding of the transformations listeners apply to speech as an input signal. Finally, we will provide concrete ideas for how to reconcile each field's constraints to reach these goals. We conclude by arguing that, although no perfect experiment can be constructed that will satisfy all constraints, a better mutual understanding of each field's approach will greatly improve experimental designs in both fields and open up new exciting avenues for research.

OVERVIEW OF RESEARCH ON SIGNAL AND SENTENCE PROCESSING

Cortical Tracking in Signal Processing Research

Cortical tracking refers to the observed alignment of rhythmic neural activity with an external periodic or quasiperiodic stimulus. It has been observed in response to both visual and auditory stimuli (Besle et al., 2011; Gomez-Ramirez et al., 2011; Luo, Liu, & Poeppel, 2010; Lakatos, Karmos, Mehta, Ulbert, & Schroeder, 2008; Lakatos et al., 2005). Although this phenomenon has received growing interest in the past decade, there is still considerable debate as to the neural causes of cortical tracking and the role it may play in various aspects of cognition (e.g., attention, temporal prediction, speech processing). Specifically, debate has centered around whether cortical tracking results from the phase-locking of ongoing, endogenous oscillations (Calderone, Lakatos, Butler, & Castellanos, 2014; Doelling et al., 2014; Giraud & Poeppel, 2012; Peelle & Davis, 2012) or whether it is the epiphenomenal result of repeated evoked responses (e.g., reflexive responses to the stimulus). There is also debate about whether cortical tracking serves a functional role in attention and speech processing, such as by acting as a mechanism for temporal prediction and segmentation (Kösem et al., 2018; Morillon & Schroeder, 2015; Calderone et al., 2014; Doelling et al., 2014; Giraud & Poeppel, 2012; Peelle & Davis, 2012; Lakatos et al., 2008), or whether it is merely a passive response to other mechanisms (Rimmele et al., 2018; Ding & Simon, 2014).

These different viewpoints are sometimes reflected in the terminology used to describe cortical tracking: Studies that argue or assume that cortical tracking involves the synchronization of ongoing oscillations often use the term "neural entrainment," as opposed to the more neutral terms cortical/neural tracking, phase coding, speech tracking, and so on (Obleser & Kayser, 2019). In this paper, we are agnostic about the neural origins and cognitive role of this phenomenon, and we therefore use the neutral term "cortical tracking" throughout.

Cortical Tracking of Speech

In this section, we briefly review the empirical and theoretical background on cortical tracking of speech. Interested readers are encouraged to explore reviews by Meyer (2018), Kösem and van Wassenhove (2017), and Obleser and Kayser (2019) for comprehensive explanations.

Much of the empirical work on cortical tracking of speech has been based on the view that it arises from the phase-locking of ongoing oscillations to events in the speech signal and that it represents an attentional or attention-like mechanism whereby periods of high neuronal excitability align with the temporal occurrence of the stimulus events to maximize processing efficiency (Giraud & Poeppel, 2012; Peelle & Davis, 2012; Lakatos et al., 2008). The idea of cortical tracking as an attentional mechanism has been theorized to support beat perception in music through the Dynamic Attending Theory (Large & Jones, 1999; Large & Kolen, 1994). According to this account, the perception of rhythm relies on the dynamic allocation of attention to points in time when the next beat is predicted to occur. The synchronization of neural oscillations to the beat is therefore a mechanism that allows for temporal predictions. In addition, cortical tracking has been observed for imagined groupings of acoustically identical periodic beats (Nozaradan, Peretz, Missal, & Mouraux, 2011), providing further evidence for its role in the perception of hierarchically organized rhythmic patterns, or meter. It also indicates that cortical tracking may reflect the segmentation of stimuli into larger units not necessarily represented acoustically (but see Meyer et al., 2020, and Tyler, 2020, for important considerations on the difference between cortical tracking of acoustic features as opposed to endogenously generated representations).

It has been argued that this type of attentional mechanism, allowing for temporal predictions through the synchronization of ongoing neural oscillations, is used for the perception of speech as well (Meyer, 2018; Ding et al., 2016; Doelling et al., 2014; Giraud & Poeppel, 2012; Peelle & Davis, 2012). Speech is a temporal signal consisting of quasiperiodic events at multiple timescales. Cortical tracking has been observed in response to many acoustic and linguistic properties of speech, including syllabic rate (Doelling et al., 2014; Peelle et al., 2013; Luo & Poeppel, 2007), the presence of prosodic intonational boundaries (Bourguignon et al., 2013), and the presence of syntactic phrases (Meyer & Gumbert, 2018; Meyer et al., 2017; Ding et al., 2016). Given that speech requires extremely fast processing, often in noisy environments, it would be beneficial for the listener to be able to preallocate attention to the points in time where important bits of signal will likely occur. In this way, the listener can ensure that this information will coincide with maximal neuronal excitability and therefore more efficient processing (Meyer & Gumbert, 2018; Morillon & Schroeder, 2015; Peelle & Davis, 2012). Speech and music would not be unique in this respect, as temporal predictions are thought to modulate attention and facilitate processing of events at predicted time locations more broadly (Nobre & van Ede, 2018), and temporal predictions in the auditory domain in particular have demonstrated the involvement of delta oscillations (Stefanics et al., 2010) similarly to the domain of language (Ding et al., 2016).

This ability to predict where important linguistic information is likely to occur could also support the temporal segmentation of speech into its linguistic units (Doelling et al., 2014; Giraud & Poeppel, 2012), such as the formation of syntactic boundaries (Meyer et al., 2017; Ding et al., 2016). In a foundational study, Ding et al. (2016) showed evidence of cortical tracking not only to periodically presented monosyllabic words but also to the two-word phrases and the four-word sentences that these words combined into. Importantly, syntactic boundaries were not marked acoustically, suggesting that the observed cortical tracking reflected a mental representation rather than an acoustic property, similar to what has been found for an imaginary meter (Nozaradan et al., 2011). If cortical tracking plays a functional role in actively predicting temporal events and in segmenting speech into units, then it may be an essential aspect of speech perception and language comprehension (Schwartze & Kotz, 2013; Peelle & Davis, 2012; Kotz & Schwartze, 2010; Ghitza & Greenberg, 2009).

Although this view has recently gained popularity, some have pointed out that what may appear as the entrainment of intrinsic oscillations to speech may in fact result from a series of evoked responses (e.g., Nora et al., 2020) or the by-product of attentional gain mechanisms (e.g., Kerlin, Shahin, & Miller, 2010; for discussions, see Ding & Simon, 2014, and Kösem & van Wassenhove, 2017). Cortical tracking would therefore consist of a passive response that plays no functional role in comprehension. Despite the difficulty of ruling out this possibility, several recent studies have provided evidence for oscillatory models that entail a more active role of cortical tracking in speech comprehension (Keitel et al., 2018; Kösem et al., 2018; Meyer & Gumbert, 2018; Zoefel, Archer-Boyd, & Davis, 2018; Meyer et al., 2017; Ding et al., 2016; Ding, Chatterjee, & Simon, 2014;

Doelling et al., 2014; Peelle et al., 2013). The idea that cortical tracking entirely reflects evoked responses is also inconsistent with the finding that neural oscillations persist at the stimulus frequency for several cycles even after the stimulus ends (Calderone et al., 2014). A third possibility is that cortical tracking does reflect the phase-locking of endogenous neuronal oscillations but that this is not itself a temporal prediction mechanism; rather, neural oscillations may constitute a processing constraint, and phase reset is induced by subcortical structures involved in the top–down temporal prediction of both periodic and aperiodic signals (Rimmele et al., 2018).

With respect to speech in particular, debate surrounds the question of whether cortical tracking reflects only low-level perception of acoustic properties of speech or whether it is actively involved in top–down speech comprehension, tracking language-specific features beyond acoustic features. One common way to address this question has been to vary the degree of speech intelligibility through acoustic manipulations, which has led to mixed results (e.g., Baltzell, Srinivasan, & Richards, 2017; Zoefel & VanRullen, 2016; Millman, Johnson, & Prendergast, 2015; Doelling et al., 2014; Peelle et al., 2013; Howard & Poeppel, 2010; Ahissar et al., 2001). One possibility is that multiple mechanisms are involved, such that cortical tracking may play different roles and track different features depending on the frequency band and the neuroanatomical source (Ding & Simon, 2014; Kösem & van Wassenhove, 2017; Zoefel & VanRullen, 2015). For instance, it has been recently proposed that cortical tracking consists of both "entrainment proper" (phase-locking to acoustic periodicities of the signal) and "intrinsic synchronicities" reflecting the endogenous generation of linguistic structure and predictions (see Meyer et al., 2020, for a clear distinction of these terms). Thus, although cortical tracking of speech has recently received much attention, its source and role are still debated, and there is still much to learn regarding its functional role in language comprehension. We will argue that cortical tracking is a useful tool for exploring psycholinguistic questions about language comprehension regardless of what neural mechanisms it may reflect and that psycholinguistic paradigms may in fact help elucidate the potential role(s) of cortical tracking in language processing and cognition more broadly.

Psycholinguistic Issues in Sentence Processing Research

Next, we will focus on the kinds of questions that have been asked in sentence processing research and the general classes of theories that have been proposed to account for psycholinguistic performance. The purpose of this section is not to provide an exhaustive review but rather to set the stage for the discussion to follow regarding how sentence processing research conceptualizes the important considerations that go into designing empirical studies.

The fundamental question that sentence processing theories try to address is how humans understand language in real time. (Of course language production is an important area of investigation as well but is beyond the scope of this review.) As the written or spoken signal unfolds, the comprehender assigns an interpretation at a number of different levels of linguistic representation: prosodic, syntactic, semantic, and pragmatic. A core assumption is that the system is "incremental," meaning that interpretations are assigned as the input is received and at all levels of representation (but see Christiansen & Chater, 2015; Bever & Townsend, 2001). Thus, upon hearing the word "The" at the start of an utterance, the syllable is categorized as an instance of the word "the," it is assigned the syntactic category "determiner," and a syntactic structure is projected positing the existence of a subject noun phrase and perhaps even an entire clause (i.e., so-called "left-corner" parsing; Abney & Johnson, 1991; Johnson-Laird, 1983). Incremental interpretation supports efficient processing because input is categorized as it is received, which avoids the need for backtracking and for holding unanalyzed material in working memory. However, incremental interpretation will often lead to "garden paths" at a number of levels of interpretation: For example, given a sequence such as "The principal spoke to the cafeteria…," readers tend to spend a long time fixating on "cafeteria" because it is implausible as the object of "speak to," a confusion that gets resolved once an animate noun such as "manager" is encountered (Staub, Rayner, Pollatsek, Hyönä, & Majewski, 2007); similarly, there is evidence from ERPs that any word can invoke a late positivity similar to a P600 component with cumulative syntactic effort, as measured by the number of parsing steps taken to parse the sentence before encountering the word (Hale, Dyer, Kuncoro, & Brennan, 2018).

Debate continues regarding the most compelling theoretical framework for explaining these and other processing effects (for a review, see Traxler, 2014). However, psycholinguists do agree that comprehenders eventually make use of all relevant information and that processing is constrained by the architectural properties of the overall cognitive system, including working memory constraints (e.g., Kim, Oines, & Miyake, 2018; Huettig & Janse, 2016; Swets, Desmet, Hambrick, & Ferreira, 2007). Recent models emphasize the need to account for the language system's tendency to construct shallow, incomplete, and occasionally nonveridical representations of the input (Ferreira & Lowder, 2016; Gibson, Bergen, & Piantadosi, 2013; Ferreira, 2003). Related approaches highlight the rational nature of comprehension, which assume that readers and listeners optimally combine the input with their rational expectations to arrive at an optimal construction of the linguistic signal, which may allow for alterations to the input in accordance with noisy channel models (Futrell, Gibson, & Levy, 2020; Gibson et al., 2013). These models are often rooted in computational algorithms that assign surprisal (the degree to which the word is expected given the preceding context) and entropy (the degree to which the word constrains upcoming linguistic content) values to each word in a sentence, reflecting how easily a word can be integrated given the left context and the overall statistics of the language (Futrell et al., 2020). Neuroimaging evidence indicates that activation in language-related brain areas correlates with difficulty as reflected by these information-theoretic measures (e.g., Russo et al., 2020; Henderson, Choi, Lowder, & Ferreira, 2016). Recent neural models of language processing locate the operation of combining two elements into a syntactic representation in Brodmann's area 44 of Broca's area, which forms a network for processing of syntactic complexity in combination with the superior temporal gyrus (Fedorenko & Blank, 2020; Zaccarella, Schell, & Friederici, 2017; for a competing view, see Matchin & Hickok, 2020).

The theoretical debates outlined above would likely be of interest to those who use cortical tracking to study auditory signal processing, just as the cortical tracking of speech is clearly relevant to psycholinguistic research. Both fields have shown interest in discovering how listeners might assign abstract linguistic structure to continuous acoustic input as it unfolds and in determining the neural correlates of spoken language processing.

BRIDGING THE TWO FIELDS

When spoken language is the signal, the studies of sentence processing and of auditory signal processing share the goal of characterizing the neural and cognitive architecture of language comprehension. However, the two areas have not extensively collaborated to address this question. Research in sentence processing makes extensive use of electrophysiological measures, especially through the use of ERPs, which have contributed greatly to our understanding of language comprehension (Swaab et al., 2012; Kutas & Federmeier, 2011; Kutas et al., 2006). Beyond the now routine use of ERPs, many psycholinguists have also adopted time–frequency analyses of EEG and magnetoencephalography data, as increases or decreases in power at various frequency bands have been found to correlate with several aspects of comprehension (for reviews, see Prystauka & Lewis, 2019; Meyer, 2018; Bastiaansen & Hagoort, 2006). The use of time–frequency analyses has enabled researchers to make fuller use of their data by including both synchronized and desynchronized neural activity, thus not discarding neural activity that is not phase-locked to a stimulus (Bastiaansen, Mazaheri, & Jensen, 2012). Yet, despite the widespread use of ERPs and time–frequency analyses of neural oscillations, the use of cortical tracking methods in particular to answer psycholinguistic questions to date is relatively rare. Importantly, cortical tracking implies a relationship between the periodicities found in neural activity and those found in the linguistic stimuli, which is different from the types of time–frequency analyses already frequently used in psycholinguistics. Strictly speaking, a power change in a certain frequency band does not imply phase-locking (and by the same token, momentary phase coherence does not imply an ongoing oscillation). As mentioned earlier, most studies that use cortical tracking of speech stem from the fields of signal processing, auditory processing, and neuroscience.

Nonetheless, there are some notable examples of research overlapping the methods and questions of these two fields. For example, Meyer and colleagues have performed several experiments that measure cortical tracking of speech using typical psycholinguistic experimental designs to answer questions about syntactic parsing, some of which we describe later in the Contributions to Psycholinguistics section (e.g., Meyer & Gumbert, 2018; Meyer et al., 2017). Similarly, Martin and Doumas (2017) have proposed a computational model linking cortical tracking to the building of hierarchical representations of linguistic structure.

However, beyond these emerging pockets of research bridging the gap between sentence processing and signal processing, the two fields remain largely independent. One of the reasons for this may be that the two take very different approaches to the study of language processing. Although many researchers who use cortical tracking methods are interested in signal processing more broadly and consider speech to be one of many naturally occurring complex signals (e.g., Rimmele et al., 2018; Morillon & Schroeder, 2015), sentence processing research typically emphasizes the linguistic properties of language and the different levels of cognitive representations that are generated during language processing, as discussed in the previous section.

As is often the case in interdisciplinary research, a major challenge lies in the discrepancies in terminology and definitions across different literatures. In particular, studies in the two fields may sometimes even differ in their definition of language comprehension (e.g., the distinction between speech perception, processing, and comprehension; see Meyer, 2018) or may not specify the degree or level of comprehension being assessed. Language comprehension entails a range of cognitive processes and levels of representations, which are sometimes left underspecified because of shallow processing (Wang, Bastiaansen, Yang, & Hagoort, 2011, 2012; Ferreira & Patson, 2007; Ferreira, 2003; Sanford & Sturt, 2002; Christianson, Hollingworth, Halliwell, & Ferreira, 2001). Thus, researchers attempting to bridge the two fields will need to be aware of how comprehension is conceptualized across studies.

More generally, the limited collaboration may stem from the different methodological constraints that the two fields typically prioritize, because of their different theoretical backgrounds. In the following sections, we summarize some of the methodological constraints and solutions that are often employed in signal processing studies that use cortical tracking methods and in sentence processing research and note how these constraints are sometimes at odds.

METHODOLOGICAL CONSTRAINTS ACROSS FIELDS

Cortical Tracking Constraints

In cortical tracking studies, there are several experimental constraints that commonly arise. Foremost among them is the requirement for long stretches of continuous, varied speech. This follows from the signal processing view that speech perception is a mathematically estimable operation that transforms speech into brain responses continuously, with various responses generally overlapping one another in time. A diverse family of techniques known as system identification is well suited to characterize such continuous input–output transformations. In the system-identification framework, an input signal x (e.g., a sound) is transformed through a system $f(x)$ (e.g., the brain)—which is not directly observable—to produce an output signal y (e.g., an EEG signal). By presenting a range of systematically varied x inputs to the system and measuring y, researchers can estimate $\hat{f}(x)$ to approximate the system that transforms input to output (e.g., the brain). Notice that these data-driven approaches do not necessarily presume a certain relationship between input (the signal) and output (the neural response) and therefore may be agnostic to the specific processes within the system that may contribute to the transformation. Instead, they tend to approach neural data with few a priori assumptions, to "discover" a relationship between the signal and the neural response. This is achieved by offering the system (the listener) various instances of the input signal of interest (e.g., spoken sentences) and measuring how the output signal (e.g., the EEG recording) responds differently at each moment. Characterizing the speech–brain system entails modeling this relationship.

Linguistic Stimulus Considerations

Most of the constraints signal processing researchers optimize for concern the stimulus, which serves as the input signal. The first such constraint is that there must be a certain degree of variability in the stimulus. Speech input is often modeled by its slow (less than ~16 Hz) power fluctuations in the acoustic envelope. The acoustic envelope reflects the perceptually salient syllabic structure of speech and empirically relates to prominent cortical ERPs, such as the N1 (Sanders & Neville, 2003). Because modeling the speech–brain system is essentially a statistical estimation problem (see Ljung, Chen, & Mu, 2020), the speech input must be varied in its properties to sample all the possibly relevant values, and it must do so without bias (or the analysis must explicitly correct for any bias). With a lack of variability and naturalism in the speech, the estimation will either be unrepresentative, reflecting the idiosyncrasies of the specific speech corpus, or it will fail to find a relationship at all.

A second constraint is that signal processing approaches may require numerous trials. Just as insufficient stimulus variability can undermine the statistical estimation described earlier, having too little data can lead to invalid estimates or a failure to find a relationship between input and output signals. In principle, there is no limit to the parameter space of this speech–brain system, but here too, many instances of each parameter must be presented to the listener. Furthermore, as in any model estimation problem, the more "free parameters" that must be characterized, the more data are usually required. System-identification approaches therefore offer great flexibility and interpretive power, but at the cost of acquiring more data and ensuring a statistically balanced array of parameters, akin to using a Latin square experimental design. A related constraint that often arises in cortical tracking studies is the need to repeat identical segments of speech multiple times. The motivation here is the same as when creating a traditional, simple ERP: An average response to multiple identical events (say, a tone) will be a more representative estimate with a higher signal-to-noise ratio than any individual response. Unsurprisingly, in single-cell auditory neurophysiology, where a signal-processing mindset has long dominated and influenced many speech-tracking EEG investigators, repeated presentations are de rigueur (e.g., in the venerable poststimulus time histogram). In some cases, the data-driven nature of system-identification techniques might compel such averaging, but better signal-to-noise will help virtually any cortical tracking measure.

A third constraint concerns the periodicity of the auditory stimulus itself. In contrast to system identification, another class of influential cortical tracking experiments manipulates the speech signal's acoustic and linguistic structures to be artificially periodic (e.g., Ding et al., 2016) and may result in stronger cortical tracking (Meyer et al., 2020; Alexandrou, Saarinen, Kujala, & Salmelin, 2018). From the signal processing perspective, this is beneficial because it allows more straightforward analysis of how the periodicity of speech input is "tracked" by the brain. Specifically, frequency-domain measures allow the investigator to focus only on those periodicities of interest with relatively high statistical power. However, linguistic events are not strictly periodic in time (Nolan & Jeon, 2014; see Beier & Ferreira, 2018, for a discussion). This tension has further relevance to questions of entrainment, particularly the hypothesis that intrinsic brain oscillations become phase-reset or otherwise temporally aligned with informative speech features. Experimentally, to identify entrainment, it may be useful to have well-defined periodicities as opposed to natural speech dynamics. However, introducing such periodicities limits the ability to determine whether entrainment occurs for natural speech and, by extension, whether entrainment plays an active role in speech comprehension outside the laboratory.

Behavioral Task Considerations

In cortical tracking paradigms, the main consideration regarding the inclusion of a behavioral task is that it should not impede continuous EEG recording or contribute significant noise to the data. Cortical tracking studies may employ a passive listening paradigm (e.g., Keitel, Ince, Gross, & Kayser, 2017; Gross et al., 2013) to obtain EEG recording that is not continually interrupted by motor movements (e.g., button presses) from behavioral tasks on the assumption that spoken language is automatically processed even if there is no offline behavioral task (e.g., in ERP studies presenting auditory sentences; van Berkum, 2004), an assumption that is sometimes held in sentence processing research as well. Relatedly, investigators may omit a behavioral task to prevent unnatural processing strategies that may add noise to the EEG data (for further discussion, see Hamilton & Huth, 2020).

In some cases, however, signal processing studies do include a behavioral task to encourage participants to attend to the auditory signal. For instance, participants may be given probe words and asked to indicate whether they heard those words on a previous trial (e.g., Keitel et al., 2018; Falk, Lanzilotti, & Schön, 2017), or they may be asked to detect semantic anomalies in the sentence (Meyer & Gumbert, 2018). Alternatively, participants may be asked to count the number of words or syllables in the presented sentences (Batterink & Paller, 2017) or to press a button every *n*th-word (e.g., fourth-word) sentence (Getz, Ding, Newport, & Poeppel, 2018). To ensure attention to the acoustic properties of the signal, cortical tracking studies may include acoustic or temporal deviation tasks, which require participants to indicate when or whether the pitch or loudness changed in the speech they heard (Zoefel et al., 2018; Rimmele, Golumbic, Schröger, & Poeppel, 2015). In investigations of language comprehension as opposed to low-level acoustic perception, an offline task is sometimes included to ensure listeners interpreted the utterance successfully, such as a self-report of the number of words participants understood in the signal (Baltzell et al., 2017; Peelle et al., 2013) or comprehension questions (Weissbart, Kandylaki, & Reichenbach, 2020; Biau, Torralba, Fuentemilla, de Diego Balaguer, & Soto-Faraco, 2015). In summary, because signal processing studies are primarily concerned with characterizing the processes that lead to comprehension in real time, behavioral tasks are often viewed as tools to encourage participants to pay attention to an input signal.

Although the experimental requirements of cortical tracking studies tend to be rather technical in nature, they do illustrate why signal processing research has long placed such great emphasis on the continuous nature of speech processing: not only because this is likely how the brain works but also because this is mathematically inherent to the most common techniques (including both time series system-identification and frequency-domain analyses). The constraints also reflect the data-driven nature of signal processing approaches, which can be theory agnostic, in part because they might require a representative and unbiased sampling of the speech–brain activity to achieve a valid result.

Psycholinguistic Constraints

In a typical sentence processing experiment, participants read or listen to sentences with manipulations relevant to the theoretical question that the experiment is designed to evaluate (e.g., sentences with grammatical, semantic, or pragmatic anomalies). Researchers then compare processing of those sentences to sentences in a baseline condition that do not contain any anomaly but are otherwise identical to the experimental sentences (i.e., "minimal pairs" that are controlled for lexical, semantic, and syntactic features). A difference in averaged behavioral response between the experimental and baseline conditions (e.g., longer RTs or reading times) would indicate processing effects that are because of the linguistic manipulation. Importantly, the experiment is designed to control for extraneous variables and to ensure that the measures reflect specific cognitive and neural mechanisms that underlie language comprehension. To address these concerns, a set of guidelines for designing the experimental stimuli and the behavioral tasks has become mainstream in psycholinguistics over the years.

Linguistic Stimulus Considerations

In sentence processing research, linguistic stimuli are typically controlled for factors that are known to influence processing to rule out potential confounds. For example, the length and frequency of words used can affect the magnitude and timing of ERPs (Strijkers, Costa, & Thierry, 2010; Hauk & Pulvermüller, 2004; King & Kutas, 1998), and therefore, word frequency is either controlled at the stimulus creation stage (e.g., selecting words with a similar frequency from a database) or statistically controlled by including frequency in a model at the analysis stage. Relatedly, function words (e.g., prepositions, determiners) evoke different neural responses than do content words (e.g., nouns, verbs): The former evokes a left-lateralized negative shift that the latter does not (Brown, Hagoort, & ter Keurs, 1999). The amplitude of the N400 response to concrete words is larger than that for abstract words, and there is greater right-hemisphere activity for concrete words (Kounios &

Holcomb, 1994). Words with a higher orthographic neighborhood density (e.g., the number of words with a similar orthographic representation, such as "lose" and "rose") or a phonological neighborhood density (e.g., "cat" and "kit") evoke greater N400 negativity than those with a low neighborhood density (Winsler, Midgley, Grainger, & Holcomb, 2018; Holcomb, Grainger, & O'Rourke, 2002).

The position of the target word in a sentence can also affect processing and therefore must be taken into consideration when designing stimuli. For example, the N400 amplitude is larger for words that occur earlier, and the effect is attenuated by word frequency (Van Petten & Kutas, 1990). Low transition probability from word to word, or even syllable to syllable, can evoke the N400 response (Teinonen & Huotilainen, 2012; Kutas & Federmeier, 2011; Cunillera, Toro, Sebastián-Gallés, & Rodríguez-Fornells, 2006). To control for transition probability, stimuli are typically cloze-normed (Taylor, 1953). In the cloze procedure, participants read fragments of the experimental sentences and are asked to provide the word(s) that best completes the sentence. The proportion of a given response out of all responses provided is the cloze probability for that response and is thought to index its predictability for the preceding context. For example, if participants read the sentence "It was a breezy day so the boy went outside to fly a _____" and 90% of them responded with the word "kite", then the word "kite" has a cloze probability of 90% and would be considered a highly predictable sentence continuation. A sentence that violates phrase structure rules or is otherwise ungrammatical (e.g., agreement errors, such as "The doctors is late for surgery") can trigger an early left anterior negativity (ELAN) as well as the P600 component (Friederici & Meyer, 2004; Friederici, 2002). By norming stimuli for acceptability, which is a proxy for sentence grammaticality that is more accessible to naive raters (Huang & Ferreira, 2020), stimuli that do or do not evoke ERPs linked to structural violations can be selected, depending on the research question. In addition, stimuli are frequently normed for typicality, plausibility, and naturalness. Stimuli that are atypical or implausible will likely evoke N400 responses, and unnatural stimuli could evoke N400 or P600 components, depending on what aspect of the linguistic content leads raters to indicate that they seem unnatural.

Behavioral Task Considerations

In addition to carefully controlling the experimental stimuli, psycholinguistic experiments typically include an offline behavioral task to verify that participants comprehended the stimuli, such as employing true–false questions (Brothers, Swaab, & Traxler, 2017), semantic judgments (Wang, Hagoort, & Jensen, 2018), or asking participants to evaluate each sentence or narrative based on their grammaticality, acceptability, or plausibility (see Myers, 2009). For research investigating lower-level language processing, such as acoustic representations, researchers have used simple detection tasks such as asking participants to monitor a particular phoneme and to press a response key when they hear that phoneme, but the use of detection tasks has declined in sentence processing research for various reasons (for a review, see Ferreira & Anes, 1994).

Some studies of speech comprehension do not include any explicit tasks besides passive listening (e.g., van Berkum, Brown, Zwitserlood, Kooijman, & Hagoort, 2005; see van Berkum, 2004, for a discussion). These paradigms circumvent issues associated with metalinguistic judgments and may prevent unnatural processing strategies (see Hamilton & Huth, 2020). They are also particularly advantageous when investigating language processing in special populations who may have impaired ability to perform additional behavioral tasks, such as some autistic individuals and children (Brennan, 2016). In studies of typical language processing in adults, however, comprehension tasks are often used because they allow researchers to directly measure the interpretation that participants have generated after processing the stimuli (Ferreira & Yang, 2019). It can be argued that comprehension tasks are crucial because passively presenting the linguistic stimuli to participants does not guarantee that they have fully analyzed the linguistic material and have generated an interpretation for it. Instead, they may engage in shallow processing and come away with an incomplete or even incorrect interpretation of the sentence (Ferreira & Patson, 2007; Ferreira, 2003; Christianson et al., 2001). Omitting a comprehension task may also encourage participants to adopt idiosyncratic goals during the experiment (Salverda, Brown, & Tanenhaus, 2011). Different task demands have additionally been shown to affect the extent to which people engage in basic linguistic processing such as resolving anaphors, structure building, and inferencing (Foertsch & Gernsbacher, 1994) as well as lexical prediction (Brothers et al., 2017). Finally, the behavioral task participants engage in can systematically influence language-related ERP components, including the N400 (Chwilla, Brown, & Hagoort, 1995; Bentin, Kutas, & Hillyard, 1993; Deacon, Breton, Ritter, & Vaughan, 1991) and the P600 (Schacht, Sommer, Shmuilovich, Martíenz, & Martín-Loeches, 2014; Gunter & Friederici, 1999).

The presence and type of behavioral task will vary depending on the research questions and goals of the study. Nonetheless, it may be necessary to consider the kind and depth of language processing that is induced in the experiment, as motivation and strategies are known to affect language comprehension (Ferreira & Yang, 2019; Alexopoulou, Michel, Murakami, & Meurers, 2017). Well-controlled linguistic stimuli and behavioral tasks enable sentence processing researchers to draw conclusions about the specific cognitive and neural mechanisms that support language comprehension, including the time course of these processes as well as the generated interpretation resulting from comprehension.

Reconciling Constraints across Fields

Sentence processing researchers who wish to include cortical tracking as a method and signal processing researchers who wish to employ more linguistic control in their stimuli both face the challenge of taking into account the methodological constraints of both fields. Some of the methodological constraints that psycholinguists must satisfy are difficult to reconcile with the constraints researchers who use cortical tracking methods reckon with. For example, psycholinguists carefully control the linguistic content of their stimuli (e.g., surprisal, plausibility, acceptability), which is tractable when the number of items is relatively small, and they avoid repeating the same item in an experimental session because of the effects of priming and learning. However, signal processing studies can require numerous trials, which is sometimes achieved through repeated exposure to the same item, which listeners could habituate to or overlearn. Similarly, signal processing studies often require long stretches of signal. It is difficult to create the number of unique experimental items following psycholinguistic conventions (e.g., stimulus norming) to generate the type of dataset that signal processing studies may require, and it is similarly difficult to control the linguistic properties of speech in lengthy recordings. Likewise, without an explicit comprehension task, the level of comprehension that took place and the participants' motivation are unclear, but signal processing studies may need to minimize interruptions and motor movements during EEG recording.

All interdisciplinary work requires researchers to draw from the methods used across multiple fields and ultimately agree on a common methodology. Because some methodological choices are mutually exclusive with others, no experiment can realistically meet all methodological standards. Instead, it is necessary to evaluate constraints from each field and then prioritize those that are most applicable to the research question at hand. In the event that conflicting constraints cannot be reconciled, it is worth explicitly acknowledging the validity of the constraints that could not be applied and briefly stating why they were not given priority (e.g., we could not use naturalistic stimuli because it was critical to our design to eliminate prosodic cues to syntax).

Although some constraints may be mutually exclusive —for example, the preference for more periodicity in the acoustic signal to measure cortical tracking, which conflicts with the pressure for speech to sound as natural as possible—there are steps that can be taken to reconcile other constraints without posing an undue burden on researchers. For example, even if stimuli cannot be normed or constructed to control for linguistic content, measures of some constructs (such as word frequency, surprisal, and entropy) can be obtained for existing stimuli using computational models (Hamilton & Huth, 2020; Weissbart et al., 2020; Brennan, 2016; Willems, Frank, Nijhof, Hagoort, & van den Bosch, 2016) and then controlled for statistically. Such an approach allows researchers to quantify these measures for naturalistic stimuli, which can be used to assess cortical tracking in everyday language comprehension (Alexandrou, Saarinen, Kujala, & Salmelin, 2020; Alexandrou et al., 2018).

It is important to note that both sentence and signal processing experiments tend to use stimuli that differ from the kinds of sentences and utterances that occur in everyday language. Experiments in both areas tend to make use of read speech, which gives researchers good control over the linguistic content of the stimuli but is easier to comprehend (Uchanski, Choi, Braida, Reed, & Durlach, 1996; Payton, Uchanski, & Braida, 1994), is produced at a lower speech rate (Hirose & Kawanami, 2002; Picheny, Durlach, & Braida, 1985; Crystal & House, 1982), and has exaggerated acoustic features relative to spontaneous speech (Gross et al., 2013; Finke & Rogina, 1997; Nakajima & Allen, 1993; see Alexandrou et al., 2020, for a discussion), which may affect processing. Further work using naturalistic utterances is required both to determine the degree to which cortical tracking occurs when listening to spontaneous speech and to assess whether sentence processing models generalize to everyday speech. Nonetheless, the estimable linguistic parameters available using computational models are compatible with the system-identification techniques commonly used in signal processing research. Parameters such as spectrotemporal, phonetic/phonemic, or linguistic properties can be included in the statistical model, for instance, in approaches that elaborate on multiple regression (Sassenhagen, 2019; Di Liberto & Lalor, 2017; Crosse, Di Liberto, Bednar, & Lalor, 2016). These can take continuous values, as with the acoustic envelope, or categorical ones, as with phonemic class. Furthermore, they can be modeled as changing smoothly through time (power) or occurring only at specific, transitory moments (e.g., sentence onsets, syntactic boundaries, prosodic breaks). However, as noted before, increasing the number of parameters also requires more data.

When the research question mandates the use of linguistically controlled stimuli, as in many sentence processing studies as well as signal processing experiments that rely on stimuli with a fixed structure, it is worth noting that the stimuli need not be generated from scratch. It has been standard practice in psycholinguistics for decades to share stimuli in an appendix or in other supplementary materials, which means entire lists of well-controlled stimuli that have already been normed are readily available in published papers. In addition, there are large freely available stimulus sets that researchers have compiled for general use, for example, a data set of cloze norms for over 3,000 English sentences (Peelle et al., 2020). Audio files for prerecorded stimuli may be found in online repositories such as the Open Science Framework or may be made available by authors upon request. Stimulus crowdsourcing—asking users of a crowdsourcing platform to generate stimuli that meet study-relevant constraints—is an additional strategy researchers can employ to alleviate the burden of stimulus generation. However, whatever the source of the corpus, the challenge of controlling stimuli, balancing factorial designs, and including filler items may lead to small numbers of trials. Although it is possible to conduct a rigorous study using cortical tracking methods with relatively few stimuli (e.g., Meyer et al., 2017, $N_{\text{items}} = 40$), achieving adequate statistical power might require compensation through using extended recording times, multiple sessions, or a larger number of test participants.

In addition, filler items are often helpful for providing listeners with a greater variability of stimulus types while at the same time reducing the likelihood that participants will overlearn the stimulus structure and, as a result, engage in shallow comprehension of the stimuli. This is particularly relevant for the assumption that neural data reflect a continuous process, as repetitive stimuli may induce shallow or atypical processing of the speech signal, in which case the function estimated by system-identification techniques may not correspond to more naturalistic processing. We return to this idea in the following section.

The behavioral task constraints across sentence processing and signal processing research can also be reconciled to quantify the level of comprehension more explicitly in cortical tracking paradigms. Adding a comprehension task to an experiment is a relatively easy way to motivate participants to engage in detailed comprehension of the stimuli. For instance, simple yes/no questions about the meaning of the stimuli encourage participants to construct elaborated semantic representations rather than attending to only the surface structure. Comprehension questions can be presented to participants in between blocks, or on the filler items only, to avoid introducing neural responses related to decision-making on the experimental trials and to ensure that motor movements do not interfere with the EEG recording. If the paradigm would not allow a comprehension task to be intermingled with the experimental trials, experimenters can motivate careful attention to the stimuli by telling participants at the start of the experiment to anticipate a memory test at the end of the session.

Speech is a continuous signal, and psycholinguists who study sentence processing are ultimately interested in understanding how listeners interpret that continuous signal. Nevertheless, there is a tendency to examine language processing through the analysis of discrete events, in part because of the conventions and analysis approaches used historically in the field (Jewett & Williston, 1971). To understand how listeners process real-time spoken input, sentence processing would benefit from adopting the methodological and analysis techniques employed in the study of signal processing for working with continuous data. Furthermore, it is far less common in sentence processing work for researchers to consider the periodicity of the signal, or variability in the amplitude envelope, which can affect neural signals. By understanding how these acoustic features impact EEG recordings, psycholinguists conducting sentence processing experiments can better separate the relative contribution of acoustic and linguistic properties of their experimental stimuli, which would allow them to draw stronger conclusions about how linguistic features (e.g., lexical ambiguity) ultimately influence comprehension.

Finally, although cortical tracking is an inherently temporal phenomenon, linguistic attributes may strongly affect which cortical areas are involved, and thus the "spatial" pattern of tracking time series across EEG scalp channels. Many neuroimaging studies using fMRI and PET show spatial cortical activation patterns that distinguish lexical category or semantics (nouns vs. verbs, concrete vs. abstract), syntax (argument structure), and numerous other features (for examples, see Rodd, Vitello, Woollams, & Adank, 2015; Moseley & Pulvermüller, 2014; Price, 2012; Friederici, 2011). Insofar as the EEG scalp activation pattern reflects (indirectly) the locations and orientations of cortical sources, controlling such linguistic variables should lead to more consistent and representative tracking analyses.

In summary, although many of the constraints associated with conducting signal processing and sentence processing research may appear to be at odds, there are reasonable compromises that can be made to reconcile methodologies from both fields. As the difficulty of collaboration between these areas is partly because of methodological differences, some of these solutions may make it easier for both sentence processing and signal processing researchers to use cortical tracking to better understand the neural and cognitive processes underlying language comprehension. In the following sections, we further elaborate on what these two fields have to gain from this collaboration and provide more detailed examples of ways to incorporate each field's methods and standards.

Contribution to Signal Processing Research

What can the study of signal processing, using cortical tracking methods, gain from developing stimuli that satisfy certain psycholinguistic constraints? Stimuli that are implausible, anomalous, or otherwise unnatural in some manner elicit ERP components (e.g., N400s, P600s, ELAN), which will affect oscillations if they occur in the same frequency band and therefore could contribute unwanted noise if not intentionally manipulated. Repetition of the same (or highly similar) sentence or the same syntactic frame throughout the study could also have unintended processing effects. Syntactic similarity across sentences produces structural priming, in which structural similarity between previous sentences facilitates processing of the current sentence (Tooley, Traxler, & Swaab, 2009; Pickering & Ferreira, 2008; Bock, 1986). Unintended priming effects should be avoided because it is unclear how structural priming of this sort might influence cortical tracking of speech or alter the EEG signal in unintended ways. Another concern is that, when a sentence template is used frequently, the listener can overlearn the template and employ a behavioral strategy that undermines the study. For example, if the task is to detect a word and the target word repeatedly occurs in the same location in the sentence, listeners could successfully circumvent the intended purpose of the comprehension task by attending only to the target region of the sentence. A shallow processing strategy of this sort would allow for high performance on the task without the need to comprehend the sentence. This problem could be avoided by including filler items with different sentence structures and varying the location of the target word within the experimental items, when possible. When the syntactic structure is highly predictable because of overlearning, it may additionally attenuate the EEG signal (Tooley et al., 2009).

Importantly, controlling for the linguistic aspects of stimuli may also help researchers determine whether cortical tracking reflects evoked responses or intrinsic oscillations. If stimuli are controlled such that we can determine when and where larger ERPs should occur, variation introduced by ERPs may be more readily dissociated from variation because of intrinsic oscillations. Through the availability of computational models, many linguistic factors can be controlled for statistically (Hamilton & Huth, 2020; Weissbart et al., 2020; Brennan, 2016; Willems et al., 2016), which would allow researchers to use lengthy, naturalistic auditory stimuli that are often required in signal processing experiments and still account for linguistic constraints. Controlling for linguistic factors that are known to induce processing difficulty or to otherwise affect language processing will yield cleaner data and will provide greater context for interpreting variations in the EEG signal.

In addition to carefully controlling the stimuli, it may be worthwhile to include an explicit comprehension task to ensure participants engage in detailed comprehension while listening to the stimuli, especially if the research aim is to test the role of cortical tracking in comprehension. As discussed in the Psycholinguistic Constraints section, listeners' strategies for comprehension can vary depending on the goal and the task demands (see Ferreira & Yang, 2019), and shallow processing can sometimes lead to underspecified or even incorrect representations (Ferreira & Patson, 2007; Sanford & Sturt, 2002), thus potentially adding noise to the neural data corresponding to these cognitive processes. It is important to acknowledge that naturalistic paradigms have numerous advantages (see Hamilton & Huth, 2020; Brennan, 2016), and it is indeed not necessary to include a comprehension task if the study's goal does not pertain to higher-level language comprehension per se (e.g., using cortical tracking methods to investigate the sequential grouping of syllables into words, not sentence or discourse-level comprehension). Nevertheless, even in this case, it is worthwhile to consider how task effects impact EEG data because any neural response that has not been accounted for has the potential to add noise. As mentioned previously, language-related ERPs have been shown to vary depending on the level of processing induced by different tasks (e.g., Chwilla et al., 1995; Bentin et al., 1993).

In selecting a behavioral task that addresses comprehension, there are a number of considerations regarding the kind of processing that is induced by the task. When appropriate, comprehension questions are ideal because they enable researchers to quantify the level of comprehension that took place, and they may be a better alternative to self-reported intelligibility because they circumvent unconscious biases. Word detection and anomaly detection tasks are useful in encouraging participants to attend to the sentences, but participants may not necessarily engage in detailed comprehension because these tasks tap into memory for the surface structure rather than the overall meaning of the sentence. Temporal or acoustic deviation tasks, in which participants indicate when or whether the pitch, loudness, or timing changed in the speech, have similar limitations to detection tasks because they only index attention to the acoustic properties of the speech signal, rather than tapping into the processing of the linguistic content of the speech stream. Furthermore, ERPs have been shown to be influenced by whether participants are instructed to pay attention to speech rhythm or syntax (Schmidt-Kassow & Kotz, 2009a, 2009b), which may also lead to overall noisier and potentially misleading EEG data.

In summary, signal processing research using cortical tracking can reap various benefits from designing stimuli and behavioral tasks that fulfill the previously described psycholinguistic constraints. If cortical tracking of speech potentially serves a functional role in speech comprehension, it would be crucial to ensure that the electrophysiological recordings reflect comprehension of the linguistic material, in which participants build syntactic structures, commit to a sentence interpretation, resolve anaphors and ambiguity, and make inferences when applicable. To this aim, including comprehension questions yields a direct measure of linguistic processing and encourages a more detailed analysis of the sentence structure and meaning. Comprehension tasks also provide an explicit goal of comprehension for participants and prevent idiosyncratic goals and strategies, which reduce noise in the data from these extraneous factors. In the data analysis stage, the use of information-theoretic measures in statistical control can be easily implemented to account for systematic noise concerning syntactic and semantic processing. A key advantage of this computational approach is that it can be used on large stretches of naturalistic uncontrolled stimuli, bolstering the goal of investigating naturalistic language processing that is an emerging trend in both signal processing and sentence processing research (see Alexandrou et al., 2018, 2020; Hamilton & Huth, 2020; Alday, 2019; Brennan, 2016). More generally, the computational modeling approach can also elucidate the role of cortical tracking in instantiating temporal predictions, as information-theoretic modeling can identify the rich linguistic information in the signal that is coded by the brain. Signal processing researchers who are interested in using cortical tracking to study predictive coding can benefit from quantifying the depth of processing that took place because predictive processing will depend on how deeply the linguistic material was processed, which is in turn influenced by the presence and type of behavioral task (for further discussion, see Kuperberg & Jaeger, 2016). Overall, the endeavor of studying auditory signal processing can be greatly augmented by accounting for linguistic aspects in the stimuli when spoken language constitutes the signal and by employing behavioral tasks that enable explicit assessment of the depth of comprehension that took place.

Contributions to Psycholinguistics

Sentence processing research has long studied syntactic ambiguity to differentiate between contrasting theoretical accounts of cognitive parsing mechanisms. In a recent study, Meyer et al. (2017) presented ambiguous sentences such as "The client sued the murderer with the corrupt lawyer" that either did or did not include a disambiguating prosodic break before the prepositional phrase. Cortical tracking in delta-band oscillations reflected syntactic phrase groupings, which frequently—but not always—corresponded to the prosodic grouping (Bögels, Schriefers, Vonk, & Chwilla, 2011; Clifton, Carlson, & Frazier, 2002; Cutler, Dahan, & van Donselaar, 1997; Shattuck-Hufnagel & Turk, 1996; Ferreira, 1993), generating new evidence that syntactic grouping biases can override acoustic grouping cues. Cortical tracking methods could be applied further using temporarily ambiguous sentences to help differentiate between sentence parsing models.

For example, Ding et al. (2016) found that listeners showed cortical tracking to syntactic phrase boundaries (e.g., cortical tracking reflects the subject noun phrase and verb phrase boundary). If tracking of syntactic boundaries generalizes beyond the stimulus materials that Ding et al. used, then using cortical tracking to temporarily ambiguous sentences should reveal the parsing mechanisms at play. Consider the temporarily ambiguous garden-path sentence "The government plans to raise taxes failed." The sentence fragment "The government plans to raise taxes" is ambiguous because the subject of the sentence is ambiguous (1).[1] "The government" could be the subject of the verb "plans" (1a), or "The government plans" could be the subject of a sentence in which "government plans" is a compound noun (1b).

1. a) $[_{S}$ $[_{NP}$ The government] $[_{VP}$ plans …]
   b) $[_{S}$ $[_{NP}$ The government plans] $[_{VP}$ …]

Before the disambiguating word ("failed"), either interpretation of the sentence is viable. Garden-path effects suggest that comprehenders initially assume the structure in 1a (MacDonald, 1993; Frazier & Rayner, 1987). The structure is initially favored at least in part because "plans" occurs more frequently as a verb (59 occurrences) than as a noun (two occurrences) in this particular context (Corpus of Contemporary American English; Davies, 2008).

Sentence processing theories disagree with respect to whether multiple structures are considered simultaneously and on where in the sentence the parser will encounter difficulty. Serial processing models (e.g., Frazier, 1987; Frazier & Fodor, 1978) build only one structure at a time, and reanalysis only occurs when the parser attempts to integrate a syntactic unit that is not compatible with the structure. In the sentence under consideration, encountering the verb "failed" would trigger reanalysis. Parallel processing models (e.g., MacDonald, Pearlmutter, & Seidenberg, 1994; Trueswell & Tanenhaus, 1994), as the name implies, generate multiple structures and narrow down the field of candidates as the parser encounters more and more disambiguating information, which means the parser should encounter the greatest difficulty during the ambiguous region of the sentence (before "failed").

Under a parallel processing model, during the temporarily ambiguous region of a sentence, at least two competing parses (1a and 1b) are actively under consideration. Crucially, the syntactic phrase boundaries differ between the two structures early on in the sentence. We would expect to see cortical tracking to phrase boundaries corresponding to each of the competing parses during the ambiguous portion of the sentence as the parser considers multiple viable candidates. In contrast, under a serial processing model, only one parse (e.g., 1a) would be considered at a time, and the delta-band oscillatory phase should indicate the parse under consideration. We would therefore predict cortical tracking to syntactic phrase boundaries that are consistent with the parse under consideration only, and we would expect delta-band oscillatory phase reset to occur once contradictory evidence is encountered. Thus, cortical tracking methods provide us with a unique opportunity to resolve some theoretical issues that have proven difficult to disentangle using common behavioral methods such as the recording of eye movements during reading (Figure 1).

In addition, signal processing studies that compare cortical tracking to attended versus unattended speech suggest that we might be able to study depth of

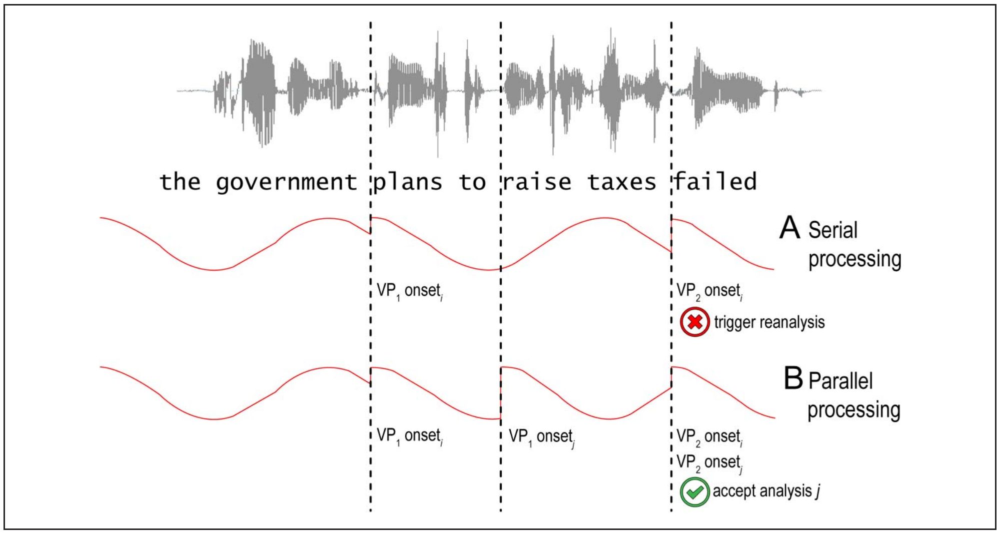

Figure 1. Illustration of predicted delta-band oscillation responses under (A) serial and (B) parallel processing accounts of sentence parsing. Cortical tracking of verb phrase boundaries indicated by a reset in oscillatory phase. The approximation of delta oscillations at 1 Hz is simplified (relative to an actual EEG recording) for clarity.

processing by measuring the degree of cortical tracking of speech. There is evidence that listeners employ shallow processing to efficiently construct a "good-enough" interpretation of the sentence (Ferreira & Patson, 2007; Ferreira, 2003; Christianson et al., 2001). For example, Ferreira (2003) presented listeners with sentences describing transitive events that either were plausible or implausible, and had active or passive syntax, and found a tendency for listeners to transform implausible passive sentences (e.g., "The dog was bitten by the man") into actives (e.g., "The dog bit the man"), thereby "correcting" the noncanonical nature of both the syntax and meaning of the sentence. The degree of cortical tracking to speech may be able to predict whether or not the listener used a heuristic strategy when processing the sentence. Specifically, we might expect weak cortical tracking to "The dog was bitten by the man" to predict a listener arriving at the incorrect but more felicitous "The dog bit the man" interpretation.

Cortical tracking would supplement not only behavioral methods but also the measures of neural activity already in use in the field of sentence processing. Cortical tracking goes beyond the use of ERPs to study language processing in that it can reveal processes occurring continuously, rather than being constrained by neural responses to discrete events. This could facilitate the process of generating linguistic stimuli, which are often required to be built around specific target words in many current designs; using cortical tracking methods, sentence processing researchers may be able to expand to more naturalistic stimuli. Cortical tracking methods also go beyond the time–frequency analyses currently in use in sentence processing research by observing neural activity that is phase-aligned to periodicities in the stimuli. As we have shown, this property may be exploited to measure how comprehenders deal with stimuli presenting ambiguous structures. Whereas the types of time–frequency analyses already in use add an invaluable piece to our understanding of language comprehension (Prystauka & Lewis, 2019), cortical tracking tools will undoubtedly add to the types of linguistic questions and paradigms that can be addressed through the recording of EEG and magnetoencephalography data.

In summary, there are exciting opportunities to investigate psycholinguistic theories by studying cortical tracking of speech and to use psycholinguistic methods to further elucidate the relationship between cortical tracking and cognitive processes associated with language processing and comprehension. As we have argued, cortical tracking may help resolve long-standing debates such as whether parsing occurs in a serial or parallel fashion, which have been left unresolved by behavioral methods and the measures of neural activity currently employed in this field.

Conclusion

The fields of sentence and signal processing both seek to understand how listeners process speech, yet collaboration between the two fields has been limited. We outlined several barriers to collaboration, with the primary ones being the different methods used across fields as well as differences in the constraints that experiments in each field must satisfy. Although some of those constraints are at odds with each other, many can be reconciled. We advocate for further collaboration across fields, which would require researchers in each area to acknowledge the experimental constraints of the other and to integrate interdisciplinary methods in their own work, whenever possible. We believe both sentence processing and signal processing research would benefit as a result, because (1) avoiding linguistic stimulus confounds would help determine whether cortical tracking reflects evoked responses or neural entrainment, (2) psycholinguists could pursue research questions that current methods (e.g., ERPs) are not well suited to address, and (3) language processing models in psycholinguistics could be better informed by incorporating findings from signal processing work. More broadly, both fields would be able to make a fuller use of their data. Signal processing researchers could reduce unwanted noise by controlling and manipulating linguistic features of their stimuli that are often overlooked and ensuring that full comprehension takes place. Sentence processing researchers could better interpret real-time processing by measuring continuous neural activity corresponding to the structure of the stimuli, rather than limiting themselves to observations of neural responses to discrete events such as particular target words. Further collaboration will give rise to new and exciting scientific discoveries of interest to both research communities.

Acknowledgments

We thank the two anonymous reviewers for their insightful comments, which helped us greatly improve our paper. Opinions, interpretations, conclusions, and recommendations are those of the authors and are not necessarily endorsed by the Department of Defense.

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Funding Information

We acknowledge support from the National Science Foundation (http://dx.doi.org/10.13039/100000001) GRFP number 1650042 awarded to E. J. B., National Science Foundation (http://dx.doi.org/10.13039/100000001) grant BCS-1650888 awarded to F. F., and National Institutes of Health grant 1R01HD100516 awarded to F. F. This work was also supported by the Office of the Assistant Secretary of Defense for Health Affairs (http://dx.doi.org/10.13039/100000005) through the Hearing Restoration Research Program, under award no. W81XWH-20-1-0485, to L. M. M.; the National Institutes of Health (http://dx.doi.org/10.13039/100000002), with grant no. R56 AG053346-02 awarded to G. R.; and the Chulalongkorn University (http://dx.doi.org/10.13039/501100002873), with grant no. CU_GIF_62_01_38_01 awarded to S. C.

Diversity in Citation Practices

A retrospective analysis of the citations in every article published in this journal from 2010 to 2020 has revealed a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience (JoCN)* during this period were M(an)/M = .408, W(oman)/M = .335, M/W = .108, and W/W = .149, the comparable proportions for the articles that these authorship teams cited were M/M = .579, W/M = .243, M/W = .102, and W/W = .076 (Fulvio et al., *JoCN*, 33:1, pp. 3–7). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance. The authors of this article report its proportions of citations by gender category to be as follows: M/M = .433, W/M = .133, M/W = .167, and W/W = .267.

Note

1. For ease of explanation, we opted to show simplified syntactic structures and only the relevant syntactic phrase boundaries in this example.

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