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14. ABSTRACT Cochlear synaptopathy is a condition where hair cell function remains viable even though synaptic connection with the auditory nerve has been severed. As a means to test for the presence of this condition, it has long been recognized that electrocochleography (ECoChG) provides an unparalleled and highly informative window into cochlear function. Experiments in animals using ototoxins and neurotoxins have allowed us to identify unique signatures of responses from hair cells and the auditory nerve, respectively. These have allowed us to identify unique metrics that are associated with synaptopathy. The goal of this project is to develop an innovative approach to use ECoChG to serve as the centerpiece of a battery of differential tests focused on cochlear synaptopathy and its perceptual sequelae. This objective aligns itself precisely with the FY18 HRRP FARA Focus Area that calls for the development of methods to assess auditory dysfunction related to synaptopathy and hidden hearing loss. The plan is to develop ECoChG measures that provide a detailed picture of the functional properties of an individual's hair cells and neural elements, and to relate this cochlear profile to auditory performance. The study includes both animal and human studies. Animal results with neurotoxins and human studies in subjects with various degrees of hearing loss are showing effects of synaptopathy on ECoChG potentials recording from the round window that can be detected with our specialized analyses. The methods have being extended to ear canal recording with should have a broader clinical applicability. New results are also showing an unexpected sensitivity of responses to distortion products of multitone stimuli to be sensitive to cochlear synaptopathy produced by neurotoxins.					
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1. INTRODUCTION

Hearing loss is typically defined as an increase in the threshold sound levels required for detection of different frequencies. Hidden hearing loss is an impairment of complex auditory function, such as understanding speech in noise, with little or no change in detection thresholds. A major hypothesis recently developed based on animal studies is that hidden hearing loss may be due to prolonged overstimulation which causes loss of auditory nerve connections to the hair cells that detect sound vibrations. In this view, detection thresholds can be maintained with a limited number of connected auditory nerve fibers, but complex processing is impaired without the complete complement of connected fibers. This mechanism of cochlear synaptopathy is difficult to observe in humans, but anatomical evidence in the form of loss of auditory nerve synapses and fibers seen post-mortem indicates that it occurs. Physiological tests to demonstrate it in living subjects are lacking. For this project, we will use the technique of electrocochleography (ECoChG) to study and describe cochlear function in detail in living subjects. ECoChG involves recording the electrical responses from the cochlea in response to sounds. The two sources of these electric potentials are the hair cell receptors that detect vibrations and the auditory nerve that transmits the information to the brain. Consequently, the technique is ideal to study the relative proportions of connections between hair cells and the auditory nerve, with any imbalance toward hair cells being an indication of cochlear synaptopathy. Our project has three aims. The first aim is to develop metrics of cochlear synaptopathy using data from animal models and apply them to human subjects recorded under similar conditions. Using animals, ototoxins or neurotoxins can be applied to selectively eliminate hair cells or neural contributions, respectively. These experiments have allowed us to identify unique signatures of responses from each source, and to develop models based on biophysical properties that generate the responses that report the magnitudes of each component. The working models are relatively early versions not specifically designed for detecting cochlear synaptopathy, and so development for this purpose is a main activity of this aim. In addition, new animal work is needed to characterize synaptopathy in the noise-exposure model that has been used in previous studies and to separate the hair cell and neural responses into their constituent components, which are not incorporated in the current models. Finally, recordings in human subjects recorded under comparable signal-to-noise conditions are available only for subjects undergoing cochlear implant surgeries. To better characterize the distribution of cochlear synaptopathy we need subjects with less compromised hearing. Consequently, recordings will be done intraoperatively in other subjects where access to the inner ear is available. The second aim is to develop the techniques for use with non-invasive recordings from the ear canal. These are needed so that they can be used routinely in the clinic. We can compare intraoperative and ear canal measurements directly by recording both at the same time. In addition, we can examine ear canal measurements in a cohort of young, normal hearing subjects, which are a good representation of many currently deployed service members. The third aim is to compare ECoChG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements. A link between the suspected synaptopathy and behavioral outcomes has been difficult to make. The ECoChG can provide a scale of synaptopathy based on objective measurements, to better test correlations between synaptopathy and the expected deficits. These subjects will also be young adults and will have audiometric hearing within the normal range. The overall product expected from this endeavor is an advanced system for evaluating cochlear function using ECoChG that can be applied to synaptopathy and hidden hearing loss or to assess cochlear function in general. This system should be scalable to the needs both of advanced diagnostics and for local measurements by clinical users at various levels of training. It is intended to provide a reliable, objective measure of hair cell and neural function on an individual level.

2. KEYWORDS

Auditory nerve

Auditory nerve neurophonic

Auditory system, Cochlea

Cochlear implants

Cochlear Microphonic

Compound Action Potential

Distortion Products

Hearing loss

Inner hair cells

Noise Exposure

Outer hair cells

Summating Potential

Synapse

Tympanic Membrane

Ear Canal ECoChG

3. ACCOMPLISHMENTS

What were the major goals of the project?

(NOTE: numbering is congruent between this section, the parallel section on accomplishments, and the figures in the attached Powerpoint file)

The overall goal is to use electrocochleography (ECoChG), or cochlear responses to sound, to measure relative degrees of hair cell and neural contributions to the recorded potentials. A reduced neural contribution is expected to be the biomarker for the presence of cochlear synaptopathy. There were three specific aims, with tasks related to each listed in the SOW.

Aim1. Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECoChG from human subjects taken under similar conditions

A1. Major Task 1. Separating the cochlear microphonic (CM) from the auditory nerve neurophonic (ANN).

Human hearing in the range for speech is dominated by low frequencies (<~1500 Hz) where neural phase-locking to the fine structure of the sound waveform is present. The evoked potential correlate of this phase-locking is the ANN, which is mixed with CM from hair cells in the fine structure of the ECoChG response. We have developed novel techniques to estimate the relative magnitudes of each in the recorded response. This separation relies on the use of fitting model based on the biophysics that produce the CM and ANN. With this model, the degree of cochlear synaptopathy, or relative paucity of neural compared to hair cell activity, should be measurable.

A1. Major Task 2 - Measuring the CM and CAP in response to high frequency sounds. Similar to Major Task 1 except that to high frequencies (i.e., >~1500 Hz) the neural component is a different feature called the compound action potential (CAP). Here, the CAP is separable from the CM in time. Because the CAP is seen early in the stimulus it is less entangled with the CM but is entangled with the summing potential (SP) which is from a mixture of sources. Thus, methods to separate the CAP and SP have been developed. To high frequencies the CM is not entangled with other potentials, so a hair cell metric is readily available.

Results from these major tasks during the past year show the methods as applied to round window (RW) recordings are also applicable to ear canal recordings. Challenges with the much less invasive ear canal recordings are the low signal-to-noise ratio (SNR) and the consequent time to obtain the large numbers of averages needed for responses to reach significance. An additional challenge is the severe low pass filtering that occurs due to tissue between the cochlear and ear canal. This filtering reduces responses at 2000 Hz compared to 250 Hz and makes responses to frequencies above 2 kHz nearly unobtainable. Fortunately, we have developed innovative ways to probe these high frequency regions using two-tone and multitone distortion products (DPs). These DPs produce *neural* and hair cell distortions in the low frequency range. The neural distortions are distinct from the otoacoustic emissions recorded with similar stimuli, which reflect basilar membrane motion and have no neural component. Thus, ear canal recordings can be used to probe the neural and hair cell function across the frequency range. We will describe these methods and results in the accomplishments section below.

A1. Major Task 3 – Development of a gerbil model of cochlear synaptopathy and identification of physiologic biomarkers of the condition using ECoChG. The goal is to identify anatomical metrics of synaptopathy following different levels of noise exposure in gerbils, and to test these known anatomical results of synaptic and hair cell losses against the physiological measurements of hair cell and neural contributions to the ECoChG.

In all of our studies, recordings from the round window of gerbils provides a test platform for human recordings using comparable stimuli. In the gerbil, very high SNRs and wide dynamic ranges allow for recordings across frequency and intensity and using lengthy experimental protocols. We can also record before and after use of neurotoxins to isolate the neural from the hair cell responses. The recent recordings in gerbils that parallel those of the new human studies from the ear canal will also be described in the accomplishments.

A1. Major Task 4. Human Intraoperative ECochG. Round window measurements of cochlear synaptopathy using CM/ANN and CM/CAP indices developed earlier and as improved in Aim 1.

New results described in the accomplishments part of the study include intraoperative recordings from the round window of human subjects to DP stimuli.

Aim2. Develop extra-tympanic recording techniques to optimize non-invasive ECochG measurement.

A2. Major Task 1. Human Intraoperative ECochG. Ear Canal recordings concurrent with round window measurements of cochlear synaptopathy.

A2. Major Task 2 Ear Canal ECochG from young adults to assess CM/ANN and CM/CAP indices from this non-invasive location.

The main human results from this past year are in the ear canal recordings from young adults.

Aim3. Compare ECochG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements

As described in previous reports this analysis has been accomplished. The ECochG data show some congruence with behavioral results, but there is not enough spread across the human results to correlate well with outcomes as predicted from cochlear synaptopathy. We will describe here that the variability in ECochG is greater than that in the behavioral results of speech in noise tests. The question then is: 1) is there no synaptopathy in this sample? or 2) is there synaptopathy that is detectable with ECochG but not reflected in behavioral tests? Our results suggest the latter is the most likely result, and that ECochG can be used to describe different patterns of hair cell and neural survival. Whether these would reflect different trajectories for hearing in the future is as yet unknown. An important next step would be to apply these analyses to subjects with greater degrees of sudden or accumulated noise exposure. Obvious subject pools would be veteran populations.

What was accomplished under these goals?

NOTE: The figures referred to are in a Powerpoint format as ‘Attachment 1 Figures.’ Figure legends are in the note section for each slide.

Aim1. Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECochG from human subjects taken under similar conditions

A1. Major Task 1. Separating the cochlear microphonic (CM) from the auditory nerve neurophonic (ANN). A1.

The reports delivered for years 1 and 2 included many details of our approach used to resolve the contributions of the ANN and CM in the combined signal. The approach is to use a deep learning algorithm to detect the presence of an ANN, and then to use modeling based the principles of the biophysics that underlie the waveform shapes independently produced for the CM and ANN to estimate the magnitudes of each present in the signal.

In figure 1 we compare examples of human ECochG to tones from the RW and ear canal. As mentioned, the round window recordings are from cochlear implant subjects while the ear canal recordings are from ‘normal hearing’ subjects, with thresholds within 20 dB of 0 dB HL from 125 Hz to 8 kHz. The RW recordings are relatively large with favorable SNR. They were obtained with 500 averages or fewer. The recordings from the ear canal are much smaller and require 2000 averages for responses to reliably reach significance relative to the noise floor. Each example shows the response to a low frequency tone (250 or 500 Hz) within the phase locking range that produces an ANN (A-C), and a high frequency tone (2 kHz) above the phase-locking range that produces a CAP as the neural contribution (D-F). The top row (A and D) are the raw responses to condensation phase. The green section defines an analysis window in the steady-state portion of

the response. For the low frequency, panel B shows the spectrum of the steady-state response with peaks at the stimulus frequency and higher harmonics (arrows). The bottom panel (C) shows the **'average cycle,'** which is the average of the cycles in the steady-state part of the response (window defined by the green panels in A). The x-axis of phase is in reference to the stimulus phase. We cannot over-emphasize the use of the average cycle, since its pattern of distortions can reveal the presence of the ANN and allow an estimate of its proportion in the overall signal. Since the CM and ANN are mixed and not easily measured separately, we developed a model based on the biophysical properties of each to estimate the amount of CM and ANN (in μV) and proportion of the response that is from the ANN.

The high frequency responses (D in each figure) from the RW of cochlear implant are usually smaller than to low frequencies but can be as large or larger in some cases. The differences across subjects relate to variation in the degree of hair cell and neural survival. In contrast, the ear canal responses to high frequencies were consistently smaller than to low frequencies (D on right, and see figure Aim1.2.1), due to the inherent low-pass characteristics of ear canal recordings. For the RW, the sum of the responses to each phase, which reduces the CM, shows a clear SP and CAP (E on left). In contrast, the N1 of the response from the ear canal, which corresponds to the CAP, is small, and there is no SP. Importantly, the average cycle of the high frequency stimulus (F) from both locations shows no evidence of an ANN as determined by the deep learning model, because of a lack of phase-locking to these frequencies.

In Fig. 2 we show similar examples from gerbil recordings from the round window. In this case the left panels are prior to application of a neurotoxin (kainic acid or KA) which is an analogue for glutamate, the neurotransmitter in the hair cell synapse to the auditory nerve, which destroys the synapse through excitotoxicity. It thus produces a gerbil analogue of cochlear synaptopathy. To low frequencies, the effect of the synaptopathy is to remove adaptation (compare panels A) and reduce the distortions (compare B and C). This removal of specific patterns of distortion in the average cycle is due to the loss of neural contributions. The spectrum is less useful because the spectra of the CM and ANN are strongly overlapping.

To high frequencies the neurotoxin removes the CAP, as expected. The SP in this case had a strong neural component, but to higher intensities the SP is dominated by asymmetric saturation of hair cell movement to the positive and negative phases of each stimulus cycle that produces a baseline shift. At this moderate intensity the average cycle of the CM is sinusoidal, but to higher intensities asymmetric saturation to the two phases is apparent.

These examples illustrate our approach to analyzing ECochG to low frequencies from different species (human and gerbil) and recording locations (RW and ear canal). Responses to low frequencies are fundamentally different from those to high frequencies due to neural phase locking, which is used by the brain to provide particularly potent timing cues for pitch, increased SNR, and sound localization. Strong similarities in results from gerbils and humans show that the biophysical principles that produce hair cell and neural responses in each can be used to meaningfully characterize the shape of the ECochG response in terms of the average cycle.

Further validation of the estimates of CM and ANN produced by our model is shown in Fig. A1.1.3. Here, we plot the proportion of ANN produced by the model against an independent estimate of the degree of distortion in the responses available from hair cell distortions alone. To do this, we created a large catalog of average cycles from CM-only responses obtained to high frequencies in gerbils. Then, for a given average cycle to a low frequency, we ran a normalized cross-correlation between it and all of the average cycles to high frequencies to identify the one with the highest correlation at its best phase lag. We then did a least square fit between the test, low-frequency average cycle and its best fit, high frequency, CM-only curve and calculated the root-mean square value of the residuals between them. With this measure a large residual indicates greater distortion compared to any possible hair cell distortion. Across the three data sets of Normal Hearing Gerbils (A), Human RW recordings (B) and Human Ear Canal (C), the results are remarkably consistent, with the proportion of ANN estimated from the model consistent with that expected from this independent measure with a correlation (r) of about 0.7-0.85. The difference is that the use of the model allows for a quantitative estimate of the amount of ANN in each case.

Aim 1. Major Task 2 - Measuring the CM and CAP in response to high frequency sounds.

To high frequencies, the CM is easily measured since it is the sole component producing the cyclic response to the stimulus (Figs 1 and 2). The CAP is also in principle easily measured as well since it occurs at the onset and has a distinct shape that resembles an action potential. From the round window of humans

(Fig. 1.1.1) and gerbils (Fig. 1.1.2) the CAP is a prominent feature amenable to measurement. However, the distinct low pass characteristic of the ear canal makes CAP recording more problematic (Fig. 1.1.1). In Fig. 1.2.1, we compare the responses to 250 and 2000 Hz from the ear canal. A major feature is that the 2000 Hz responses lie well below the line of equality (dashed black), with a small response on average of only 0.067 μ V (mean -23.4 \pm 5.2 dB re 1 μ V), compared to 0.44 μ V at 250 Hz (-7.1 \pm 3.0 dB). Two cases did not have a response to 2 kHz that was significantly above the noise floor (open circles). A second point is that the correlation between the two frequencies was significant ($p=0.0046$) but small ($r^2=0.21$). Whether this variation is due to differential attenuation from tissue characteristics between the cochlea and ear canal or to actual variation in hair cell survival is not clear. Less than 10% of the responses to 2 kHz showed a measurable CAP. Finally, there is no possibility of obtaining responses to frequencies higher than 2 kHz, as these are commonly below the level of detection. Thus, responses to tones are not a fruitful way to use ECoChG from the ear canal.

Click stimuli are commonly used to characterize the SP and CAP, under the assumption that the SP is exclusively a hair cell response. We have extensively characterized the SP in gerbils and from the RW of human CI subjects, and find it be a highly complex signal composed of contributions from OHCs, IHCs, and spiking and dendritic components of the auditory nerve, all of which have distinct polarities and time courses. To a brief stimulus like a click there is little chance to accurately estimate the contributions of each. In addition, clicks are largely high frequency stimuli, and as mentioned from the ear canal high frequencies are selectively attenuated. In Fig. 1.2.2, we show that, as in previous studies, a grand average of 33 responses to clicks from different subjects yields the characteristic shape of an SP followed by CAP. However, three subjects had no discernible response to the clicks, and in the remainder the patterns varied widely. Thus, clicks do not offer a clear path out of the dilemma of poor SNR at the ear canal particularly to high frequencies. However, we will show in section A2.2 that we are developing sensitive methods to estimate neural contributions to high frequency stimuli using two-tone and multi-tone stimuli.

A1. Major Task 3 – Development of a gerbil model of cochlear synaptopathy and identification of physiologic biomarkers of the condition using ECoChG.

Fig. 1.1.2 describes our major approach to this task. As has been described in earlier reports we have also developed a gerbil synaptopathy model using noise exposures.

A1. Major Task 4. Human Intraoperative ECoChG. Round window measurements of cochlear synaptopathy using CM/ANN and CM/CAP indices developed earlier and as improved in Aim 1.

Fig. 1.1.1 describes our major approach to this task.

Aim2. Develop extra-tympanic recording techniques to optimize non-invasive ECoChG measurement.

A2. Major Task 1. Human Intraoperative ECoChG. Ear Canal recordings concurrent with round window measurements of cochlear synaptopathy.

Instead of the challenging task of two-channel intraoperative recording including from the low SNR region of the ear canal we have been concentrating on a separate series of ear canal recordings described below.

A2.2. Major Task 2 Ear Canal ECoChG from young adults to assess CM/ANN and CM/CAP indices from this non-invasive location.

In last year's report, we described ear canal ECoChG to tones from 14 subjects. Here, we update this information to 38 subjects. The subjects are young adults all have normal thresholds over the usual range of audiometric frequencies (250 Hz – 8 kHz, HL thresholds <20 dB). For these analyses, one subject was excluded due to a technical issue discovered later

Fig. 2.2.1 shows the distributions of CM and ANN estimated from the average cycles of each subject to 250 Hz stimulus. In A, the CM can be seen to vary from about 1 μ V (0 dB) to 0.1 μ V (-20 dB). The ANN is smaller, ranging from about -0.3 μ V (-10 dB) to less than 0.03 μ V (-30 dB). The size of the CM is not a proxy for the size of the ANN, as there is little relationship between the two. However, the proportion of the responses that is the ANN does scale with the size of the CM. This result was also seen in gerbils and reflects

the fact that the CM continues to grow with intensity over a wider range than the ANN, which saturates to lower intensities. Finally, panel C shows that the larger the ANN, the greater its proportion.

These results indicate that the range of CM and ANN measured across young adults to low frequencies is about 20 dB. A smaller absolute or proportional measure of the ANN may indicate relative degrees of cochlear synaptopathy.

For high frequencies, measuring the neural contribution through the CAP is highly challenging from the ear canal ECoChG, as described above. However, we have embarked on studies to characterize a unique measurement for this purpose. This measurement is of the responses to DPs produced by two tone or multitone stimuli. Such DPs in otoacoustic emissions have been extensively used to characterize outer hair cell function. However, otoacoustic emissions occur due to the outer hair cell motor-type function that produces non-linear basilar membrane properties that generate fluid waves that back-propagate from the oval window through the middle ear to the tympanic membrane. In contrast, ECoChG to DPs has a strong neural component due to the ANN produced by the low-frequency F2-F1 components. We and others have characterized these potentials in gerbils and conclusively demonstrated that 1) the peaks related to the F2-F1 frequency to low intensities are exclusively neural in nature, but to high intensities are mixed neural and hair cell, and 2) the potentials arise from the characteristic frequency (CF) regions of the F1 and F2 primaries, rather than the low frequency region of the F2-F1 frequencies. The data to support these conclusions are shown in Fig 2.2.2, which have been in previous reports. Responses to a multi-tone stimulus containing six primary frequencies between 4-8 kHz produce a family of F2-F1 responses in the spectrum of a low-intensity stimulus that are larger than to the primaries themselves (A). These F2-F1 responses are entirely neural because they are absent after treatment with KA. The KA does not affect the responses to the primaries, showing these are from the CM while the F2-F1 responses represent the ANN. To higher intensities (not shown) the F2-F1 responses are also produced by hair cell distortions. By observing the change in response as the KA spreads through the cochlea we observe that the ANN that produces the F2-F1 peaks are derived from auditory nerve fibers connected to IHCs that have CFs associated with the primaries rather than the lower CF regions associated with the F2-F1 frequencies themselves. In Fig. 2.2.2B, the top panel is the time course of the loss of the CAP to different stimulus frequencies as the KA spreads. It shows that the CAP is removed in a tonotopic pattern starting from high CF regions and extending to low, consistent with the spread of KA. The bottom panel shows that the responses to the F2-F1 frequencies correspond to when the KA reaches the region of the primary frequencies, i.e., the ANN disappeared as the KA knocked out the CAP to the 4 and 8 kHz frequencies rather than to lower frequencies.

We have extended the observations to the RW in CI subjects (e.g., Fig 2.2.3A) and to the ear canal in young normal hearing adults (e.g., Fig. 2.2.3B). In all of these examples there are clear peaks to the F2-F1 frequencies. We have recently been systematically characterizing the ear canal responses to a range of F2-F1 frequencies and to different frequencies of primaries. In Fig. 2.2.4A, we show the size of the peaks relative to the noise floor for two different F1 frequencies and a range of F2 frequencies from 200 to 900 Hz higher than the F1. The error bars are standard deviations from four ears across two subjects. The F2-F1 peaks are small but well above the noise floor for all but the lowest frequencies. In terms of SNR, the responses are relatively flat across F2-F1 frequencies, indicated that there is no preferred frequency within this range. The fact that two high frequency carriers produce these responses indicate that DPs analysis can be applied to the entire audible frequency range thus avoiding the issue of the low pass filtering characteristics of ear canal ECoChG.

Thus, with this technique ECoChG can potentially provide frequency-specific information about hair cell and neural survival, not currently available with any other method. DP otoacoustic emissions provide information about outer hair functional integrity, but not about neural survival. Auditory brain stem and frequency following responses reflect auditory nerve integrity but are affected by central gain due to decreased inhibition in auditory nuclei following loss of inputs. Click responses from the ear canal are not frequency-specific and are highly attenuated by the low-pass filtering relative to the inputs.

Aim3. Compare ECoChG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements

In last year's report, we described how we had started concurrent measures of ECoChG and speech-in-noise test, and present preliminary data from 14 subjects. Here, we update this information to 38 subjects.

There are two behavioral tasks involved, which are modulation masking release (MRM) and spatial masking release (SRM). Both of these speech in noise tests are hypothesized to be affected by cochlear synaptopathy. The subjects had normal thresholds over the range of audiometric frequencies (250 Hz – 8 kHz,

thresholds <20 dB HL). The audiograms of the 36 included subjects are shown in Figure 3.1. One of the 38 subjects was eliminated because the audiogram at 8 kHz fell slightly outside the inclusion range. Another was omitted because the ECoChG had a technical fault. In addition to the range from 0.25-8 kHz which was the target range, higher frequencies of 10, 12 and 16 kHz were also tested. As can be seen, the audiograms from these young normal hearing subjects showed a range of hearing loss to these higher frequencies.

The MRM task measures the improvement in speech perception threshold when speech-shaped maskers are modulated vs. unmodulated, and the SRM task measures the improvement when the target speech is spatially separated (45 degrees to either side) from the masker speech (please note that more complete experimental details for the behavioral experiments were provided in the Q7 report). The ECoChG is the ear canal responses from the same subjects to 250 Hz and 2 kHz tones. From the 250 Hz tones we can measure the CM and ANN as in Fig. A1.1.1 and A2.1.1. Results are shown in Fig. 3.2. In A, there is no significant relationship between masking releases in the spatial and modulation domains. These indicate that the measure tap into different brain mechanisms. Then, neither type of masking release is associated with the ANN proportion in low frequency sounds (B and C).

Possible reasons for a lack of correlation between the ANN and behavioral measures are that none of these young subject's measure to date has much synaptopathy to low frequencies to detect. This result is in contrast to CI subjects where the presence of cochlear synaptopathy is strongly indicated. The sum of these results is consistent with current thinking in the field, which that synaptopathy may be more strongly present once a degree of permanent hearing loss occurs. Another possibility is that the range of the speech detection thresholds to the individual stimuli (e.g., to the modulated and unmodulated maskers) are small for both stimuli, less than about 6 dB (data not shown), and the range of masking release in both the modulation and spatial measures is less than 10 dB (A in Fig. 3.2). In contrast, there is a 20 dB spread in the amount of ANN across subjects (see Fig. 2.2.1A). Thus, the ECoChG may be a more sensitive measure of synaptopathy in subjects this sample of subjects that may map onto a greater propensity for future hearing difficulties.

We note our new tests using DPs are not yet well-enough characterized to apply to behavioral results. Our current studies as described above are geared to assessing the best stimuli to use to efficiently obtain results across a wide range of stimulus frequencies.

A significant relationship between ECoChG and behavior is shown in Fig. A3.3. In this case we plot the hearing threshold as a function of the CM at 2 kHz for frequencies that are higher than the usual audiometric range. There is a clear negative correlation, such that a large CM is associated with a better threshold. This result indicates that being able to probe higher frequencies with ECoChG through the use of DPs may yield even greater behavioral relevance.

What opportunities for training and professional development has the project provided?

A postdoctoral fellow was trained in the anatomy and physiology of the auditory system, which was a new direction for him. His major projects were to develop the deep learning model to identify the presence of the ANN and to improve the analytic model for estimating quantities of CM and ANN in a given ECoChG response to a low frequency tone. Most recently he has extended this model to characterize different shapes of the CM-only average cycles as representing different patterns of interaction from different cochlear locations.

A research assistant who performed the animal studies is currently applying to medical school.

How were the results disseminated to communities of interest?

A podium talk on the DPs in ECoChG from gerbils and human subject was presented at the (virtual) Association for Research on Otolaryngology Midwinter meeting in February 2022 (files are in the attachments). A paper on the SP and CI subjects was published in JARO (attached).

What do you plan to do during the next reporting period to accomplish the goals?

A major goal of our no cost extension is to publish our major findings. Four manuscripts are currently in preparation:

1. Cochlear synaptopathy in human CI subjects
2. ECoChG to tones from the Ear Canal of young adults with normal hearing: Characterization of correlation with speech-in-noise tests and audiological thresholds.
3. ECoChG to two-tone and multi-tone DPs from the RW of gerbils and human CI subjects
4. ECoChG to two-tone and multi-tone DPs from the ear canal of young adults with normal hearing.

Experimental plans are to continue characterizing the ECoChG to DPs from the ear canal. Our goal is to develop a set of stimuli that can efficiently characterize a subject's neural function across the frequency range. The stimuli currently planned are for a given F1 frequency, e.g., 2 kHz, to be presented with a multitone stimulus with of six F2 frequencies spaced 150 Hz apart. In this way the following series of F2-F1 frequencies will be created: 150 Hz (six pairs), 300 Hz (5 pairs), 450 Hz (4 pairs), 600 Hz (3 pairs), 750 Hz (2 pairs) and 900 Hz (1 pair). The multiplication of pairs is expected to produce larger responses, so that both amplitude and 'cut-off' frequency, i.e., the number of pairs required to see a response, can be obtained. This stimulus can be repeated with different F1 frequencies. In addition, to further demonstrate that the responses from the ear canal is neural we are performing experiments with simultaneous and forward maskers under the assumption that neural potentials will be masked while hair cell potentials will not.

4. IMPACT

What was the impact on the development of the principal discipline(s) of the project?

The identification of cochlear synaptopathy as a potential cause of hearing loss is a recent development based on animal studies. There is some anatomical evidence that it occurs in humans, but physiological and behavioral correlates have proven elusive. Our studies have an impact because our finding of substantial cochlear synaptopathy in cochlear implant subjects is the clearest demonstration that it exists in humans in the setting of considerable permanent hearing loss. Our analyses of the CM, ANN, CAP and SP are among the most sophisticated for characterizing and understanding neural hair cell and neural architecture through ECoChG. We are expanding our findings to the ear canal in novel ways that hold the potential to describe the hair cell and neural architecture across the frequency range. This approach holds the possibility of overcoming the main barriers to the use of ECoChG as a clinical tool, which are low SNR and low frequency cutoff.

What was the impact on other disciplines?

Nothing to report

What was the impact on technology transfer?

Nothing to report

What was the impact on society beyond science and technology?

Nothing to report

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

The change to using DP analysis to probe neural and hair cell responses to high frequency was required to overcome the limitations of ear canal ECoChG including low SNR and cut-off frequency.

Actual or anticipated problems or delays and actions or plans to resolve them

None anticipated

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report, all ACURO, HRPO, IRB and IACUC protocols are in place and experiments are progressing.

6. PRODUCTS

Publications, conference papers, and presentations

Two presentations at the midwinter meeting at the Association for Research on Otolaryngology Midwinter meeting (virtual) in February, 2021. The title of the abstract is "Probable Cochlear Synaptopathy in Cochlear Implant Subjects." A manuscript was submitted to Science Translation but not reviewed, it will be resubmitted to a more specialized hearing journal (Hearing Research).

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)

Nothing to report

Technologies or techniques

In the year 1 report we included our code for separating the ANN from the CM, as attachments. Additional code has been developed and is fully available.

Inventions, patent applications, and/or licenses

Nothing to report

Other Products

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- What individuals have worked on the project?

Name:	Douglas Fitzpatrick
Project Role:	<i>PI</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	3.6 calendar months
Contribution to Project:	<i>Dr. Fitzpatrick has supervised the performance of animal experiments and performed and supervised data analysis</i>
Funding Support:	<i>National Institutes of Health Advanced Bionics Corporation</i>

Name:	<i>John Grose</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	3.6 calendar months
Contribution to Project:	Dr Grose is assisting in the preparation of the IRBs and piloting ear canal and tympanic membrane recordings for other protocols that can provide relevant information to guide our data collection once approval is granted.
Funding Support:	<i>NA</i>

Name:	<i>Kendall Hutson</i>
Project Role:	<i>Neurotologist</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	6 calendar months
Contribution to Project:	<i>Dr, Hutson is performing or supervising the animal experiments</i>
Funding Support:	<i>National Institutes of Health Advanced Bionics Corporation</i>

Name:	<i>Raymond Haggerty</i>
Project Role:	<i>Post Doctoral fellow</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	12 calendar months
Contribution to Project:	<i>Dr. Haggerty is improving the models used to separate the CM and ANN and the CM and CAP. He is using the models to analyze existing data sets and new data sets using noise exposures in gerbils and ultimately in new human recordings</i>
Funding Support:	<i>None</i>

Name:	<i>Meredith Hamby</i>
Project Role:	<i>Research Assistant</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	12 calendar months
Contribution to Project:	<i>Meredith performs animal and human ECoChG</i>
Funding Support:	<i>None</i>

Name:	<i>Stephan Pulver</i>
Project Role:	<i>Research Assistant</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	2.76 calendar months
Contribution to Project:	<i>Stephan does the cochlear dissections necessary for confocal imaging of gerbils cochleas</i>
Funding Support:	<i>None</i>

Name:	<i>Oliver F. Adunka</i>
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Project Role:	<i>Neurotologist</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	0.12
Contribution to Project:	<i>Dr. Adunka has provided institution oversight for development and attainment of IRB approvals and protocol setup for The Ohio State University.</i>
Funding Support:	<i>National Institutes of Health-NIDCD (U01)- 20%</i>

Name:	<i>William J. Riggs</i>
Project Role:	<i>Audiologist</i>
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	2.4
Contribution to Project:	<i>Dr. Riggs has worked on IRB approvals and protocol setup for The Ohio State University.</i>
Funding Support:	<i>National Institutes of Health-NIDCD (U01)- 20%</i>

- **What other Organizations were involved as partners?**

- The Ohio State University
- Ohio State is the site where most of the recordings from non-CI subjects are occurring. They have recorded from 11 new subjects since full approval was obtained.

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

None

CURRENT-COMPLETED SUPPORT FOR DOD

LNAME, FNAME: Fitzpatrick, Doug

* W81XWH1910609, newly active funding

*1U01DC018920-01, newly active funding

CURRENT/ACTIVE

Grant Title/Main PI's Last Name/Grant Number:	Measurements of Cochlear Synaptopathy Using Electrocochleography/Fitzpatrick/ W81XWH1910609
Effort (Calendar Months):	3.6 cal mon, 30% effort
Funding Agency:	DOD
Grants Officer Name & the Address of Funding Agency:	Susan M Dellinger 1077 Patchel St., Bldg 1077 Fort Detrick, MD 21702
Project Dates:	08/15/2019-08/14/2022
Funding Amount:	
Project Goals:	The proposed work is targeted to unraveling the ECoChG signal with the intent of improving accuracy of the feedback.
Specific Aims:	Aim 1: Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECoChG from human subjects taken under similar conditions Aim 2: Develop extra-tympanic recording techniques to optimize non-invasive ECoChG measurement Aim 3: Compare ECoChG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements
Overlap	NONE

Grant Title/Main PI's Last Name/Grant Number:	Clinical Utility of Residual Hearing in the Cochlear Implant Ear/Adunka/1U01DC018920-01
Effort (Calendar Months):	1.8 cal mon, 15% effort
Funding Agency:	NIH/NIDCD
Grants Officer Name & the Address of Funding Agency:	Kelly Anne King NSC BG RM 8309 6001 Executive Blvd, Rockville, MC 20852
Project Dates:	08/01/2020-07/31/2025
Funding Amount:	
Project Goals:	The present proposal aims to improve cochlear implant outcomes for candidates with residual hearing. These hearing remnants often pose a barrier for potential candidates. Consistent preservation and subsequent ipsilateral electric acoustic stimulation will help to make this technology available to more patients suffering from substantial levels of hearing loss.
Specific Aims:	Therefore, the present protocol seeks to answer two critical clinical questions in cochlear implantation: (Specific Aim 1) Are cochlear implant electrode insertions using Electrocochleography (ECoChG) feedback better for achieving hearing preservation (HP) and (Specific Aim 2) is combined ipsilateral EAS better than non-HP (conventional) cochlear implantation among CI candidates with substantial residual hearing (EAS candidates).
Overlap:	NONE

Grant Title/Main PI's Last Name/Grant Number:	The Optimization of Electrocochleography (ECochG) for Intra-Operative Monitoring and Post-Operative Management/Fitzpatrick
Effort (Calendar Months):	7.02 cal mon, 58.55 % Effort
Funding Agency:	Advance Bionics Corporation
Grants Officer Name & the Address of Funding Agency:	Advanced Bionics AG Laubisruetistrasse 28 8712 Stäfa Switzerland
Project Dates:	10/01/2018-09/30/2021
Funding Amount:	
Project Goals:	The proposed work is targeted to unraveling the ECochG signal with the intent of improving accuracy of the feedback.
Specific Aims:	N/A
Overlap:	Effort will be reduced on this contract to accommodate the proposed effort on all pending grants.

Grant Title/Main PI's Last Name/Grant Number:	Spatial Hearing in Complex Sound Fields/ Freyman/ R01DC001625
Effort (Calendar Months):	1.08 cal mon,9% effort
Funding Agency:	NIH/ University of Massachusetts at Amherst
Grants Officer Name & the Address of Funding Agency:	N/A
Project Dates:	07/01/1992-/03/31/2021
Funding Amount:	
Project Goals:	The goal of this project is to advance the scientific understanding of binaural and spatial hearing in reverberant environments and apply this knowledge to the special problems faced by those with asymmetric hearing, leading ultimately, to better, evidence based treatment approaches for these individuals.
Specific Aims:	The aim is to examine the responses of neurons to stimuli used in perceptual studies of the precedence effect in an animal model.
Overlap	NONE

COMPLETED

None

CURRENT-COMPLETED SUPPORT FOR DOD

LNAME, FNAME: Grose, John

- * **W81XWH1910609, newly active funding**
- * **R01-DC001507, recently completed**
- * **R01-DC014460, recently completed**

CURRENT/ACTIVE

Grant Title/Main PI's Last Name/Grant Number:	Measurements of Cochlear Synaptopathy Using Electrocochleography/Fitzpatrick/W81XWH1910609
Effort (Calendar Months):	3.6 cal mon, 30% effort
Funding Agency:	DOD
Grants Officer Name & the Address of Funding Agency:	Susan M Dellinger 1077 Patchel St., Bldg 1077 Fort Detrick, MD 21702
Project Dates:	08/15/2019-08/14/2022
Funding Amount:	
Project Goals:	The proposed work is targeted to unraveling the ECoChG signal with the intent of improving accuracy of the feedback.
Specific Aims:	Aim 1: Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECoChG from human subjects taken under similar conditions Aim 2: Develop extra-tympanic recording techniques to optimize non-invasive ECoChG measurement Aim 3: Compare ECoChG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements

COMPLETED

Grant Title/Main PI's Last Name/Grant Number:	Complex sound analysis in normal and impaired ears/Grose/R01-DC001507
Effort (Calendar Months):	6.3 cal mon, 52.5% effort
Funding Agency:	NIDCD
Grants Officer Name & the Address of Funding Agency:	Castilla Mcnamara 31 Center Dr. Bethesda, MD 20892-2320
Project Dates:	12/01/1992-08/31/2019

Funding Amount:	
Project Goals:	The goal of this project is to provide a multi-faceted framework within which significant advances will be made in understanding supra-threshold deficits occurring in the presence of audiometrically normal hearing.
Specific Aims:	1. To test the hypothesis that older listeners with audiometric hearing within normal limits have auditory deficits consistent with compromised eighth nerve function. 2. To test the hypothesis that the fidelity of envelope encoding of complex stimuli declines with age and hearing loss. 3. To test the hypothesis that spectro-temporal integration of speech glimpses declines with age.
Overlap:	

Grant Title/Main PI's Last Name/Grant Number:	Factors influencing the behavioral assessment of hearing during infancy and childhood/Buss/R01-DC014460
Effort (Calendar Months):	.6 cal mon, 5% effort
Funding Agency:	NIDCD
Grants Officer Name & the Address of Funding Agency:	Eric Nunn 31 Center Dr. Bethesda, MD 20892-2320
Project Dates:	04/01/2015-03/31/2020
Funding Amount:	
Project Goals:	The long-term goal of this research is to identify the factors responsible for immature auditory behavior in infants and children, and to develop techniques for differentiating the contributions of these factors in individual listeners.
Specific Aims:	1: Test the hypothesis that self-generated noise elevates detection thresholds in young listeners, particularly at low frequencies. 2: Evaluate central auditory processing and general cognitive factors limiting performance of young listeners In developmental psychoacoustics, effects related to central auditory processing and general cognitive factors are often described in terms of 'efficiency'. 3: Evaluate novel procedures for improving behavioral assessment of hearing in infants, toddlers, and 'hard-to-test' children with hearing loss
Overlap:	

PREVIOUS-COMPLETED SUPPORT FOR DOD

LNAME, FNAME: Hutson, Ken

*** W81XWH1910609, newly active funding**

CURRENT/ACTIVE

Grant Title/Main PI's Last Name/Grant Number:	Spatial Hearing in Complex Sound Fields/Freyman/R01DC001625
Effort (Calendar Months):	1.08 cal mon, 9% effort
Funding Agency:	University of Massachusetts at Amherst/NIDCD
Grants Officer Name & the Address of Funding Agency:	Edward Myrbeck 31 Center Dr. Bethesda, MD 20892
Project Dates:	04/01/2016-03/31/2021
Funding Amount:	
Project Goals:	N/A
Specific Aims:	The aim is to examine the responses of neurons to stimuli used in perceptual studies of the precedence effect in an animal model
Overlap:	

Grant Title/Main PI's Last Name/Grant Number:	Measurements of Cochlear Synaptopathy Using Electrocochleography/Fitzpatrick/ W81XWH1910609
Effort (Calendar Months):	6 cal mon, 50% effort
Funding Agency:	DOD
Grants Officer Name & the Address of Funding Agency:	Susan M Dellinger 1077 Patchel St., Bldg 1077 Fort Detrick, MD 21702
Project Dates:	08/15/2019-08/14/2022
Funding Amount:	
Project Goals:	The proposed work is targeted to unraveling the ECochG signal with the intent of improving accuracy of the feedback.
Specific Aims:	Aim 1: Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECochG from human subjects taken under similar conditions Aim 2: Develop extra-tympanic recording techniques to optimize non-invasive ECochG measurement Aim 3: Compare ECochG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements
Overlap:	If awarded effort will be reduced on Electrocochleography: Basic Science and Clinical Utility

Grant Title/Main PI's Last Name/Grant Number:	The Optimization of Electrocochleography (ECochG) for Intra-Operative Monitoring and Post-Operative Management/Fitzpatrick
Effort (Calendar Months):	4.92 cal mon, 41 % Effort
Funding Agency:	Advance Bionics Corporation
Grants Officer Name & the Address of Funding Agency:	Advanced Bionics AG Laubisruetistrasse 28 8712 Stäfa

	Switzerland
Project Dates:	10/01/2018-09/30/2021
Funding Amount:	
Project Goals:	The proposed work is targeted to unraveling the ECochG signal with the intent of improving accuracy of the feedback.
Specific Aims:	N/A
Overlap:	Effort will be reduced on this contract to accommodate the proposed effort on all pending grants.

COMPLETED

None

PREVIOUS-COMPLETED SUPPORT FOR DOD

LNAME, FNAME: Brown, Kevin

***1U01DC018920-01, newly active funding**

CURRENT/ACTIVE

Grant Title/Main PI's Last Name/Grant Number:	Clinical Utility of Residual Hearing in the Cochlear Implant Ear/Adunka/1U01DC018920-01
Effort (Calendar Months):	0.36 cal mon, 3% effort
Funding Agency:	NIH/NIDCD
Grants Officer Name & the Address of Funding Agency:	Kelly Anne King NSC BG RM 8309 6001 Executive Blvd, Rockville, MC 20852
Project Dates:	08/01/2020-07/31/2025
Funding Amount:	
Project Goals:	The present proposal aims to improve cochlear implant outcomes for candidates with residual hearing. These hearing remnants often pose a barrier for potential candidates. Consistent preservation and subsequent ipsilateral electric acoustic stimulation will help to make this technology available to more patients suffering from substantial levels of hearing loss.

Specific Aims:	Therefore, the present protocol seeks to answer two critical clinical questions in cochlear implantation: (Specific Aim 1) Are cochlear implant electrode insertions using Electrocochleography (ECoChG) feedback better for achieving hearing preservation (HP) and (Specific Aim 2) is combined ipsilateral EAS better than non-HP (conventional) cochlear implantation among CI candidates with substantial residual hearing (EAS candidates).
Overlap:	NONE

COMPLETED

None

CURRENT-COMPLETED SUPPORT FOR DOD

ADUNKA, OLIVER F.

- * W81XWH1910609, newly active funding
- *1U01DC018920-01, newly active funding
- *Cochlear Americas, completed
- * R01DC008581, completed

Current

Grant Title/Main PI's Last Name/Grant Number: Measurements of Cochlear Synaptopathy Using Electrocochleography/Fitzpatrick/ W81XWH1910609

Effort (Calendar Months): 0.12 cal mon, 1% effort

Funding Agency: DOD

Grants Officer Name & the Address of Funding Agency: Susan M Dellinger 1077 Patchel St., Bldg 1077 Fort Detrick, MD 21702

Project Dates: 08/15/2019-08/14/2022

Funding Amount:

Project Goals: The proposed work is targeted to unraveling the ECoChG signal with the intent of improving accuracy of the feedback.

Specific Aims: Aim 1: Develop metrics of cochlear synaptopathy using data from animal models and apply them to ECoChG from human subjects taken under similar conditions

Aim 2: Develop extra-tympanic recording techniques to optimize non-invasive ECoChG measurement

Aim 3: Compare ECoChG measures of cochlear synaptopathy to audiometric and speech-in-noise measurements

Overlap: NONE

Grant Title/Main PI's Last Name/Grant Number: Clinical Utility of Residual Hearing in the Cochlear Implant Ear/Adunka/1U01DC018920-01

Effort (Calendar Months): 0.14 cal mon, 1.68% effort

Funding Agency: NIH/NIDCD

Grants Officer Name & the Address of Funding Agency: Kelly Anne King NSC BG RM 8309 6001 Executive Blvd, Rockville, MC 20852

Project Dates: 08/01/2020-07/31/2025

Funding Amount:

Project Goals: The present proposal aims to improve cochlear implant outcomes for candidates with residual hearing. These hearing remnants often pose a barrier for potential candidates. Consistent preservation and subsequent ipsilateral electric acoustic stimulation will help to make this technology available to more patients suffering from substantial levels of hearing loss.

Specific Aims: Therefore, the present protocol seeks to answer two critical clinical questions in cochlear implantation: (Specific Aim 1) Are cochlear implant electrode insertions using Electrocochleography (ECoChG) feedback better for achieving hearing preservation (HP) and (Specific Aim 2) is combined ipsilateral EAS better than non-HP (conventional) cochlear implantation among CI candidates with substantial residual hearing (EAS candidates).

Overlap: NONE

Title: Outcomes in Adults with Mixed or Conductive Hearing Loss Implanted with the Bonebridge

Time Commitments: 0.0 calendar

Supporting Agency: Med-EL

Address:

Contracting/Grants Officer: NA

Performance period: 11/18/2019-12/31/2020

Level of funding:

Project Goals: The major goals of this project are to 1) assess safety and effectiveness of the BONEBRIDGE implant in adults with mixed or conductive hearing loss, and 2) assess post-operative audiometric and speech perception outcomes with BONEBRIDGE, compared to unaided preoperative performance as well as report on intraoperative experience.

Specific Aims: NA

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Title: The Ohio State University Neurofibromatosis Type 2 Clinic

Time Commitments: 0.0 calendar

Supporting Agency: Children's Tumor Foundation

Address:

95 Pine Street, 16th Floor

New York, NY 10005

Contracting/Grants Officer: Heather Radtke

Performance period: 01/01/2020 – 12/31/2020

Level of funding:

Specific Aims: The Ohio State University NFCN Affiliate Clinic supports NF activities that will benefit patient care and the local NF Community. Stipends to the clinic provide continued support of the local NF2 Crew in the organization and hosting of their annual gathering in Columbus, Ohio. The NF2 Crew is an online-based support community for patients and family members (or loved ones) with NF2.

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Title: Cochlear Implantation during Vestibular Schwannoma Removal or During Labyrinthectomy Surgery for Treatment of Meniere's Disease

Time Commitments: 0.0 calendar

Supporting Agency: Advanced Bionics AG

Address:

Laubisrutistrasse 28

Stafa, ZH 8712

Contracting/Grants Officer: Mary Orshan

Performance period: 10/22/2018 – 10/22/2020

Level of funding: Providing cochlear implant devices only (total market value), no other funding is being received

Project Goals: The purpose of this study is to determine longitudinal benefits of listening with a cochlear implant placed during the time of tumor removal for patients with a vestibular schwannoma and/or with patients undergoing a labyrinthectomy for treatment of Meniere's disease

Specific Aims: The specific aim is to determine the effectiveness of cochlear implantation for a specific patient population with single-sided hearing loss using a battery of tests and questionnaires: Detection Testing Determination, Speech Perception Testing, Sound Localization Testing, Speech, Spatial and Qualities of Hearing Scale, and Nijmegen Cochlear Implant Questionnaire.

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Title: Neural Encoding and Auditory Processing of Electrical Stimulation in Pediatric Cochlear Implant Users

Time Commitments: 0.12 calendar

Supporting Agency: NIH

Address:

NIH

9000 Rockville Pike

Bethesda, MD 20892

Contracting/Grants Officer: Christopher Myers

Performance Period: 04/01/2019-03/31/2024

Level of Funding:

Project Goal: To 1) understand neural encoding and processing of electrical stimulation in children with cochlear nerve deficiency (CND), and 2) develop an effective, evidence-based clinical practice managing this unique patient population.

Specific Aims: Aim 1. To determine the effects of poor cochlear nerve survival on neural representation of electrical stimulation in the cochlear nerve. Aim 2. To determine the effects of poor cochlear nerve survival on cortical neural encoding of temporal and spectral cues.

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Title: Vestibular Oriented Research Meetings

Time Commitments: 0.0 calendar

Supporting Agency: NIH

Address:

NIH

9000 Rockville Pike

Bethesda, MD 20892

Contracting/Grants Officer: Edward Myrbeck

Performance Period: 03/15/2019 – 02/28/2022

Level of Funding:

Project Goal: To establish an annual vestibular oriented research meeting.

Specific Aims: Aim 1: Create and host a 3-day vestibular oriented research meeting. Aim 2: Create and host two 1-day satellite meetings.

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Completed

Title: Clinical Evaluation of the Cochlear Nucleus® CI532 Cochlear Implant in Adults

Time Commitments: 0.0 calendar

Supporting Agency: Cochlear Americas

Address:

13059 E. Peakview Avenue

Centennial, CO 80111

Contracting/Grants Officer: Christine M. Menapace

Performance Period: 03/07/2017- 03/31/2020

Level of funding:

Project Goals: To evaluate pre- and post-implantation speech recognition in quiet and noise scores in the implanted ear alone and to evaluate pre- and post-implantation Health Utility (HUI).

Specific Aims: The specific aims are to determine the group mean CNC word recognition in quiet measured at 6 months post-sound processor activation in the best unilateral condition compared to the group mean score obtained in the pre-operative, unilateral aided –ear to be implanted condition, to determine the group mean AzBio sentence in noise score measured at 6 months post-sound processor activation in the best unilateral condition compared to the group mean score obtained in the pre-operative, unilateral aided –ear to be implanted condition, and to determine the group mean HUI3 score measured at 6 months post-sound processor activation in the best unilateral condition compared to the group mean score obtained in the pre-operative, unilateral aided –ear to be implanted condition.

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

Title: Infant-directed Speech and Language Development in Infants with Hearing Loss

Time Commitments: 0.6 calendar

Supporting Agency: NIH/NIDCD R01DC008581

Address:

NHLBI Center for Scientific Review

6701 Rockledge Drive

Room 1040-MSC 7710

Bethesda, MD 20892-7710

Contracting/Grants Officer: Eric Nunn

Performance period: 08/14/2015 – 06/30/2020

Level of funding:

Project Goals: To determine how real-world language input affects language development in infants with hearing loss and to determine the underlying factors of infant-directed speech (IDS) that might facilitate language development in these infants.

Specific Aims: The specific aims are 1) To assess the quantity and quality of real-world speech directed to infants with hearing aids (HAs) and cochlear implants (CIs) relative to normal hearing (NH) peers. We will use the Language Environment Analysis (LENA) system to obtain real-world IDS and adult-directed speech (ADS) samples from the homes of CI, HA, and NH infants and perform quantitative (e.g., amount of IDS in a day) and qualitative (mean F0 of IDS vs. ADS) measurements on a representative sample of the speech input; 2) To determine direct and indirect relations between properties of IDS and language outcomes. We will assess infants' speech processing efficiency and obtain several language outcome measures; 3) To determine the effects of IDS on novel word learning in infants with PHL compared to NH peers. We will assess CI, HA, and NH infants' ability to learn novel words in IDS and ADS conditions from 9 to 27 months after receiving a CI or HA; and 4) To determine which acoustic characteristics of IDS facilitate novel word learning in NH infants under conditions of natural speech and spectrally degraded speech. We will test word learning in NH infants using pitch-, timing-, and vowel-altered stimuli under varying levels of spectral degradation (unprocessed, 32 channel, 16 channel, 8 channel).

Overlap: No scientific or budgetary overlap with the proposed PRMRP proposal

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: N/A

QUAD CHARTS: A new quad chart is attached

9. APPENDICES

1. Figures for the 'Accomplishment' section in Powerpoint format (w legends in notes).
2. Poster presented at ARO.
3. Podium presentation at ARO.
4. Quad Chart