Welcome
Catherine Palmer, PhD, Academy President
Linda Hood, PhD, ARC 2020 Chair

AN/ANSD: Current Status, Clinical Issues, Future Directions
Linda Hood, PhD, ARC 2020 Chair
Professor, Department of Hearing and Speech Sciences, Vanderbilt University

Patients with auditory neuropathy (AN)—also referred to as auditory neuropathy spectrum disorder (ANSD), auditory synaptopathy, and auditory neuropathy/dys-synchrony (AN/AD)—present unique challenges to clinicians in relation to audiological evaluation and management. Patients vary widely in speech understanding and communication ability, with difficulty understanding speech-in-noise. Test results often present a mismatch with behavioral audiometric thresholds, which is a characteristic of hearing losses affecting synaptic and neural function. Physiological responses are key to accurate identification and monitoring of patients over time. Various mechanisms underlie AN and characteristics such as etiology, age at onset, genetics, and multiple system involvement vary among patients.

Management approaches should be individualized with consideration of individual variation and the possibility of change over time. Many patients with accurately characterized AN demonstrate success with cochlear implants. Trial with amplification is recommended prior to consideration of implantation. Areas of discovery, including accurate differential diagnosis, understanding of synaptic and neural mechanisms, genotype/phenotype relationships, and contributions of cochlear and cortical evoked potentials. Advances in each area will promote accurate clinical evaluation and management of infants, children, and adults with AN.

Sound Coding in the Auditory Nerve: Toward New Diagnostic Tools
Jean Luc-Puel, PhD
Professor University Montpellier
Institute for Neurosciences of Montpellier

Auditory nerve fibers (ANFs) convey acoustic information from the sensory cells to the brainstem using an elaborated neural code based on both spike timing and rate. As the stimulus tone frequency increases, time coding fades and ceases, resulting in high-frequency tone encoding relies mostly on the spike discharge rate. Here, we will recapitulate our recent single unit data from gerbil’s auditory nerve to highlight the most relevant mode of coding (spike timing versus spike rate) in tone-in-noise.

We report that high-spontaneous rate (SR) fibers driven by low-frequency tones in noise can phase lock ~30 dB below the level that evoked a significant elevation of the discharge rate. For high-frequency tone, the low-threshold/high-SR fibers reach their maximum discharge rate in noise and do not respond to tones, whereas medium- and low-SR fibers are still able to respond to tones making them more resistant to background noise.
Based on these findings, we first discuss the ecological function of the ANF distribution according to their spontaneous discharge rate. Based on ouabain-induced ANF loss, we furthermore point out the poor synchronization of the low-SR ANFs, accounting for the discrepancy between ANF number and the amplitude of the compound action potential of the auditory nerve after ouabain. Finally, we proposed a new diagnostic tool to assess low-SR fibers, which does not rely on the onset response of the ANFs.

10:00–10:15 am  
**Break**

10:15–11:00 am  
**Cochlear Deafferentation in Noise- and Age-Related Hearing Loss: Basic Observations and Translation to Human**
Sharon Kujawa, PhD  
Associate Professor, Harvard Medical School  
Director of Audiology Research and Senior Scientist, Massachusetts Eye and Ear

After decades of focus on the sensory component of noise- and age-related hearing loss, animal studies have more recently turned attention to neural status, identifying loss of hair-cell communications with cochlear neurons as an early event for both etiologies. Losses with age are gradually progressive throughout the lifespan, and widespread throughout the cochlea. After noise, losses are sudden and can be progressive, changing the way ears and hearing age, long after the exposure has stopped.

The basic result has been documented in every mammalian species in which it has been studied, including compelling observations in age-graded human temporal bones, where the degeneration appears even greater than that seen in laboratory animals. Here, we provide an update on our basic observations of these degenerative processes and progress toward human translation. Work supported by grants from the National Institutes of Health (NIH/NIDCD), Department of Defense and Office of Naval Research.

11:00–11:45 am  
**AN/ANSD: Assessment in Infants and Toddlers**
Yvonne Sininger, PhD  
Professor Emeritus, University of California Los Angeles  
C&Y Consulting, Santa Fe, New Mexico

Infants who have failed newborn screening and toddlers with abnormal auditory development make up the majority of audiological patients with ANS. Assessment of these patients is based on objective measures. The ways in which ANS is manifested in audiological test batteries will be reviewed and discussed in relation to the physiology. Appropriate use of Auditory Brainstem Response, Cochlear Microphonic recordings, Otoacoustic Emissions, Middle Ear and Acoustic Reflex measures will be emphasized. Finally, interpretation of auditory electrophysiologic tests for assessment and differential diagnosis of ANS will be discussed.

11:45 am–2:00 pm  
**Questions and Discussions**  
Morning Speakers

12:00–1:15 pm  
**Sponsored Lunch by Phonak**  
Mentoring/Collaboration Breakout Groups  
Poster Presentations

1:15–2:15 pm  
**Electrophysiology in Patients with Gene Mutations Related to AN/ANSD**
Rosamaria Santarelli, MD, PhD  
Professor, Department of Neurosciences, University of Padova
Auditory neuropathy (AN) is a disorder characterized by disruption of the temporal coding of acoustic signals in auditory fibers with consequent impairment of auditory perceptions dependent on temporal cues. The most well-known forms of AN are due to gene mutations and the mechanisms believed to be involved are functional alterations at pre- and post-synaptic sites, including neurotransmitter release from ribbon synapses, spike initiation in auditory nerve terminals and the neural dys-synchrony accompanying demyelination and axonal loss, all resulting in impairment of auditory nerve discharge in response to acoustic stimuli.

Alterations of cochlear receptor activity and of auditory nerve discharge can be identified in patients with AN by using transtympanic electrocochleography (ECochG). ECochG findings help to define objectively the sites of auditory neural dysfunction as affecting inner hair cell receptor summating potential or compound action potential, the latter reflecting disorders of ribbon synapsis and auditory nerve fibers. The identification of specific gene mutations combined with typical electrophysiological patterns may be the key-factor in revealing how the failure of different molecular processes underlies the varieties of AN. Moreover, elucidation of the physiopathological mechanisms and site of lesion help to predict the outcome of cochlear implantation or hearing aid use in patients with AN related to different gene mutations.

2:15–3:00 pm

**Psychophysics and Bimodal Hearing in AN/ANSD**
Sterling Sheffield, AuD, PhD
Assistant Professor, Department of Speech, Language, and Hearing Sciences
University of Florida

Management of auditory neuropathy spectrum disorder (ANSD) remains challenging and research continues to seek effective treatment with differing professional opinions on the benefits of hearing aids and cochlear implants. In this presentation, temporal processing, spectral processing, and speech recognition data collected in adults with ANSD, normal-hearing thresholds, and sensorineural hearing loss will be compared to illustrate group effects and hearing aid, cochlear implant, and bimodal hearing effects. Temporal processing was evaluated with gap detection and voice-onset time discrimination. Spectral processing was evaluated with a spectral modulation detection task and consonant discrimination. Speech recognition was evaluated with words and sentences in quiet and in noise. Results indicate better performance on all tasks with bimodal hearing for both adults with sensorineural hearing loss and with ANSD.

3:00–3:15 pm

**Break**

3:15–4:00 pm

**Speech-Evoked Cortical Responses in Infants and Children With and Without Hearing Loss**
Kristen Uhler, PhD
Chair, Audiology, Speech Pathology, and Learning Services, Children’s Hospital Colorado
Associate Professor, Physical Medicine and Rehabilitation, Otolaryngology, and Psychiatry
University of Colorado Anschutz Medical Campus
Children’s Hospital Colorado

The presentation will focus on the outcomes from a recently developed, objective, non-invasive index (evoked potential) of infant speech perception to be employed shortly after hearing aid fitting and its potential impact for shaping habilitation strategies. The presentation will describe the relationship of a speech-evoked potential and how it relates to later behavioral speech discrimination abilities measured at nine months of age. The language outcomes will be provided for a subset of toddlers from their longitudinal study.
The presentation will share both normative data, as well as a cohort of infants with hearing loss across the trajectory of the project, and will discuss theoretical approaches, relationships between evoked potentials and behavior, and progress toward an automatic response detection algorithm. Potential expansion of this non-invasive measure of speech discrimination to individuals with Auditory Neuropathy will be explored via case studies.

Gene Therapy for Genetic Hearing Loss
Lawrence Lustig, PhD
Professor and Chair, Department of Otolaryngology-Head and Neck Surgery
Columbia University Medical Center/New York Presbyterian Hospital

Gene therapy has undergone significant advances towards the treatment of genetic hearing loss. Initial studies focussed on methodologies and viral constructs that would be successful for adequate delivery to the appropriate cells of the inner ear. Newer virus subtypes as well as methodologies that allow the delivery of larger genes have greatly accelerated the advances in this field the point that there are now several start-up companies focused on gene therapy for genetic hearing loss. This talk will summarize the state of the field and focus on two forms of hearing loss, a subtype of Usher Syndrome (3a) and a form of non-syndromic deafness due to loss of function of Otoferlin.

Questions and Discussions
Afternoon speakers

Closing Remarks
Linda Hood, PhD, ARC 2020 Chair