Electrocochleography (ECochG): New Applications of an Old Procedure

- Introduction: Historical overview of ECochG
- Review of test protocol for ECochG recording
- Review of test electrode options for ECochG recording
- Clinical applications of ECochG in adults
- Clinical applications of ECochG in the diagnosis of auditory neuropathy spectrum disorder (ANSD)

Original Description of Electrocochleography (ECochG)


E. Glen Weaver, Ph.D. (October 16, 1902 — September 4, 1991)

ELECTROCOCHLEOGRAPHY: 83 Years Old and Still Clinically Important!

- 1930: Wever & Bray (CM in cat)
- 1935: Fromm et al (CM in human)
- 1950: Tasaki (AP in human)
- 1954: Davis (SP)
- 1960: Yoshie, Portmann (TT CM & AP)
- 1967: Coats, Eggermont, Gibson (Dx of MD)
- 1974: Hall (I/O)
- 1990: Various (Auditory Neuropathy)
- 1996: Multiple contributors

Time in Years
ELECTROCOCHLEOGRAPHY:
Generators

- Cochlear microphonic (CM)
  - Outer hair cells
  - Receptor potentials

- Summating potential (SP)
  - Inner hair cells (> 50%)
  - Outer hair cells
  - Organ of Corti

- Action potential (AP)
  - Afferent fibers in distal 8th cranial nerve
  - Spiral ganglion
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ECochG TEST PROTOCOL (1)

<table>
<thead>
<tr>
<th>Stimulus Parameters</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>Clicks</td>
</tr>
<tr>
<td>Duration</td>
<td>0.1 ms</td>
</tr>
<tr>
<td>Rate</td>
<td>7.1/sec; slower if needed or faster if possible</td>
</tr>
</tbody>
</table>
| Polarity            | Alternating (for SP and AP)  
|                     | Rarefaction and condensation (for CM) |
| Intensity           | Maximum or lower |
| Transducer          | Insert |
| Masking             | Never needed (Components are biological markers for ear-specific response) |
**ECochG TEST PROTOCOL (2)**

<table>
<thead>
<tr>
<th>Acquisition Parameters</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplification</td>
<td>75,000 or less</td>
</tr>
<tr>
<td>Analysis time</td>
<td>5 or 10 ms</td>
</tr>
<tr>
<td>Sweeps</td>
<td>500 or less (depends on SNR)</td>
</tr>
<tr>
<td>Filters</td>
<td>10 to 1500 Hz</td>
</tr>
<tr>
<td>Notch filter</td>
<td>Never</td>
</tr>
<tr>
<td>Electrodes</td>
<td></td>
</tr>
<tr>
<td>Option 1</td>
<td>Fz to trans-tympanic needle</td>
</tr>
<tr>
<td>Option 2</td>
<td>Fz to tympanic membrane</td>
</tr>
<tr>
<td>Option 3</td>
<td>Fz to Tiptrode</td>
</tr>
</tbody>
</table>

**ECochG Electrode Options:*

_The Closer to the Cochlea, the Better_

![Diagram showing electrode options]

**ECochG is a Near Field Response**

![Diagram showing near field response]
Sub-Dermal Needle Electrode for Trans-Tympanic Promontory ECoG Recording
**Electrocochleography (ECochG): New Applications of an Old Procedure**

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**Electrocochleography (ECochG): Clinical Applications in Adults**

- Enhancement of wave I in ABR measurement with air- and bone conduction click stimulation to:
  - Enhance inter-wave latency analysis
  - Confirm ear-specific test findings (biological marker)
  - Minimize the need for masking non-test ear
- Intra-Operative Neurophysiological Monitoring
  - Prompt documentation of cochlear status
  - Enhance inter-wave latency analysis
  - Minimize interference of electrical artifact
- Diagnosis of Meniere’s disease

---

**ECochG in Diagnosis of Meniere’s Disease:**
Abnormally Large SP/AP Ratio

Coats AC (1981). The summating potential in Meniere’s and non-Meniere’s ears. Archives of Otolaryngology, 107, 199-208


ELECTROCOCHLEOGRAPHY: Selected Papers
(Published on 9/9/14 at www.nlm.nih.gov with key words “Meniere’s Disease” and “electrocochleography” showed > 400 publications)

- Auditory dysfunction in tinnitus
- Cochlear and round window (Soundbridge) implants
  - Round window and intra-cochlear recordings
  - Intra-operative verification of cochlear implant function
  - Intra-operative documentation of low frequency cochlear function during electrode insertion
  - Prediction of speech perception outcomes
- Diagnosis of auditory neuropathy spectrum disorder (ANSD)
  - Differentiation of pre- versus post-synaptic auditory dysfunction

ELECTROCOCHLEOGRAPHY (ECochG):
More Recent Clinical Applications

- Auditory dysfunction in tinnitus
- Cochlear and round window (Soundbridge) implants
  - Round window and intra-cochlear recordings
  - Intra-operative verification of cochlear implant function
  - Intra-operative documentation of low frequency cochlear function during electrode insertion
  - Prediction of speech perception outcomes
- Diagnosis of auditory neuropathy spectrum disorder (ANSD)
  - Differentiation of pre- versus post-synaptic auditory dysfunction
Clinical Applications of Electrocochleography (ECochG) in Audiology Today

- Introduction: Historical overview of ECochG
- Review of test protocol for ECochG recording
- Review of test electrode options for ECochG recording
- Clinical applications of ECochG in adults
- Clinical applications of ECochG in the diagnosis of auditory neuropathy spectrum disorder (ANSD)
- Summary, Questions & Answers

Strategies for Identification and Diagnosis of Auditory Neuropathy Spectrum Disorder (ANSD):

Normal OAEs

[Graph showing OAEs for different frequencies and ears]

Strategies for Identification and Diagnosis of Auditory Neuropathy Spectrum Disorder (ANSD):

No ABR and Large Cochlear Microphonic

[Graph showing ABR and Cochlear Microphonic for different frequencies and ears]
Essential Role of Electrocochleography (ECochG) in the Diagnosis and Management of Auditory Neuropathy Spectrum Disorder (ANSD)

Cerebello-pontine angle (CPA)
Internal Auditory Canal (Auditory Nerve)
Spiral ganglion cells
IHC - 8th CN Synapse (glutamate)
Inner hair cells
Outer hair cells

Identification, Diagnosis, and Management of Auditory Neuropathy Spectrum Disorder (ANSD): Prevalence Estimations

- Well baby (normal) population
  - Between 0.006% to 0.03% (Korver et al. JIPORL, 76 (12), 2012)
  - Up to 3/10,000 births
- Children with hearing loss
  - ~ 5% (Bielicki et al, JIPORL, 76 (11), 2012)
  - ~ 4% (Dadhia et al, JAMA Otol H&NS, 139, 2013)
  - Mittal et al. JIPORL, 76, 2012
    - 5.3% of all children with hearing loss
    - 14% of children with severe-to-profound hearing loss

The Cross-Check Principle in Pediatric Audiology
(Jerger J & Hayes D. Arch Otolaryngol 102: 1976)
The Cross-Check Principle Pediatric Audiology  
(Jerger J & Hayes D. Arch Otolaryngol 102: 1976)  
What’s missing from the test battery?

<table>
<thead>
<tr>
<th>Test Battery:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavioral audiometry</td>
</tr>
<tr>
<td>Immittance (impedance) measurements</td>
</tr>
<tr>
<td>✓ Typanometry</td>
</tr>
<tr>
<td>✓ Acoustic reflexes (contralateral only with SPAR)</td>
</tr>
<tr>
<td>Auditory brainstem response (brainstem-evoked response audiometry or BSER)</td>
</tr>
<tr>
<td>✓ Click stimulus air conduction</td>
</tr>
<tr>
<td>✓ Click stimulus bone conduction</td>
</tr>
</tbody>
</table>

We have found than simply observing the auditory behavior of children does not always yield an accurate description of hearing loss...  
"The basic operation of this principle is that no result be accepted until it is confirmed by an independent measure."

**Testing Battery:**
- **Behavioral audiometry**
- **Immittance (Impedance) measurements**
  - Typanometry
  - Acoustic reflexes (contralateral only with SPAR)
- **Auditory brainstem response (Brainstem-evoked response audiometry or BSER)**
  - Click stimulus air conduction
  - Click stimulus bone conduction

---

**Strategies for Identification and Diagnosis of Auditory Neuropathy Spectrum Disorder (ANSD): Confusing Terminology**

- "Auditory neuropathy" coined in 1996 by neurologist Arnold Starr
  - Normal outer hair cell function by OAE or ECoG and abnormal afferent auditory function (abnormal ABR)
  - 8/10 patients with "AN" had generalized peripheral neuropathy
  - Post-synaptic, i.e., type II AN (Starr et al, 1996)
  - Pre-synaptic, i.e., type I AN (Starr et al, 1996)
- Auditory dysynchrony (Berlin et al, 2001)
- Auditory neuropathy senso stricto (Rapin & Gravel, 2002, 2006)
- Auditory synaptopathy/auditory neuropathy
  - May also include pure inner hair cell dysfunction
  - Site of dysfunction does not indicate type of dysfunction
- Auditory neuropathy spectrum disorder (ANSD)

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**Identification, Diagnosis, and Management of Auditory Neuropathy Spectrum Disorder (ANSD): Characteristic Pattern of Auditory Findings**

- Auditory brainstem response (ABR)
  - Absent ABR with no wave I
- OAEs
  - Normal or present initially
  - 98% still have OAEs over time (Sanvelbhaa et al. IJPORL, 77, 2013)
- Cochlear microphonic (CM) OAEs
  - Present with rarefaction versus condensation stimuli
- Absent acoustic reflexes
- Pure tone audiometry
  - Variable from normal to rising pattern to no response
- Speech audiometry
  - Poor word recognition relative to hearing thresholds
  - Very poor speech perception in noise
In June 2008, Deborah Hayes invited a panel of experts to meet in Como, Italy at the NHS 2008 Conference to develop Guidelines for the Identification and Management of Infants and Young Children with Auditory Neuropathy.

The panel consisted of:

- Yvonne Sininger, Ph.D.
- Arnold Starr, M.D.
- Christine Petit, M.D., Ph.D.
- Gary Rance, Ph.D.
- Barbara Cone, Ph.D.
- Kai Uus, M.D., Ph.D.
- Patricia Roush, Au.D.
- Jon Shallop, Ph.D.
- Charles Berlin, Ph.D.

Electrocochleography (ECochG):
Diagnosis of Auditory Neuropathy Spectrum Disorder

Tests of cochlear hair cell function

- Otoacoustic emissions (OAEs)
- Cochlear microphonic (ECochG and ABR)
  - CM may be present when OAEs are absent (e.g., with middle ear dysfunction)

Tests of auditory nerve function

- ABR for high intensity click stimulation (e.g., 80 to 90 dB nHL) with separate averages for:
  - Rarefaction stimulus polarity
  - Condensation stimulus polarity

Additional tests

- Acoustic reflex measurement (generally acoustic reflexes are absent in ANSD)
- Suppression of otoacoustic emissions (abnormal, e.g, no suppression in ANSD)

Identification and Diagnosis of Auditory Neuropathy Spectrum Disorder (ANSD):
Minimal Test Battery (2010 ANSD Guidelines)

Perinatal Diseases

- Hyperbilirubinemia
- Hypoxic insults
- Ischemic insults
- Prematurity

Neurological Disorders

- Demyelinating diseases
- Hydrocephalus
- Immune disorders, e.g., Guillain-Barre syndrome
- Inflammatory neuropathies
- Severe developmental delay

Essential Role of Electrocochleography (ECochG) in the Diagnosis and Management of Auditory Neuropathy Spectrum Disorder (ANSD): Medical diagnoses (1)
### Essential Role of Electrocochleography (ECochG) in the Diagnosis and Management of Auditory Neuropathy Spectrum Disorder (ANSD): Medical diagnoses (2)

- **Neuro-metabolic diseases**
- **Genetic and Hereditary Etiologies**
  - Family history
  - Connexin mutations, e.g., GJB3 (D66del)
  - Otoferlin (OTOF) gene
  - Non-syndromic recessive auditory neuropathy
  - Hereditary motor sensory neuropathies (HMSN), e.g., Charcot-Marie-Tooth syndrome
  - Leber’s hereditary optic neuropathy
  - Waardenburg’s syndrome
  - Neurogenerative diseases, e.g., Friedreich’s ataxia
- **Mitochondrial disorders, e.g., mitochondrial enzymatic defect**

### Other Procedures Important in the Diagnosis and Management of Auditory Neuropathy Spectrum Disorder (2008 Guidelines)

- **Components of assessment**
  - Pediatric and developmental history
  - Otologic evaluation, plus
    - Imaging of cochlea with CT
    - Imaging auditory nerve with MRI
  - Medical genetics evaluation
  - Ophthalmologic evaluation
  - Neurological evaluation to assess:
    - Peripheral nerve function
    - Cranial nerve function
  - Communication assessment

### ANSD: Histopathology (Starr)

![Histopathology Diagram](image-url)
Comprehensive Assessment of Auditory Neuropathy Spectrum Disorder (ANSD): MRI of Auditory Nerve

- Brainstem and inner ear abnormalities in children with auditory neuropathy spectrum disorder and cochlear nerve deficiency. Huang et al. (UNC). American J Radiol, 31, 2010
  - CND was identified in 33.0% of children and 26.9% of ears with ANSD
  - Significantly more patients with bilateral CND had intracranial abnormalities than those with unilateral CND (60.0% versus 15.8%).

  - Cochlear nerve deficiency can be seen by electrophysiological evidence and may be a significant cause of unilateral AN.
  - Inclined sagittal MRI of the internal auditory canal is recommended for the diagnosis of this disorder.

Auditory Neuropathy Spectrum Disorder ANSD:
Defining Site of Dysfunction is the Key to Accurate Diagnosis and Effective Management

![Diagram of auditory system](image)

- Action Potential (AP)
- Summating potential (SP)
- Cochlear microphonic (CM)

ECochG in ANSD:
Refining diagnosis of "site of lesion" (1)

  - 8 subjects (with AN versus 16 normal subjects
  - AN subjects between 5 and 48 years of age
  - Diagnosis based on presence of DPOAEs and absence of ABR (incl. wave I)
  - Enlarged CM in AN patients (Starr et al, 2001; Santarelli & Arslan, 2002)
- Etiology
  - Hereditary (3) Immunological (3)
  - Degenerative (1) Congenital (1)
- ECochG measures included
  - CM SP AP
  - Adaptation of AP determined by AP elicited by a first click versus AP elicited by a train of 10 rapid clicks (2.9 ms ISI)

- 14 subjects (7 male and 7 female) with AN versus 2 normal subjects
- AN diagnosed between 3 and 24 months of age
- Diagnosis based on large CM potentials and absence of ABR (incl. wave I)
- Genetic etiology for 6 subjects
- Severe to profound audiometric thresholds for all subjects
- All subjects received cochlear implants
- Purpose of study was to better define physiology mechanisms of AN to guide management (including cochlear implantation)
- ECochG recorded with
  - Non-inverting ("active") electrode near round window "golf club" electrode with inverting electrode on ipsilateral earlobe
- ECochG in AN consistent with:
  - Pre-synaptic mechanism (abnormal SP) = good EABR and CI benefit
  - Post-synaptic mechanism = poor or absent EABR and poor CI benefit


- Trans-tympanic ECochG for 10 children with ANSD versus matched group with SNHL
- Examined
  - Thresholds
  - Latencies
  - Amplitude ratio between CAP and SP
- ECochG can add valuable information for a precise differential diagnosis of AS/AN
  - When the CAP/AP ratio falls below 1.0 patients can be diagnosed AS/AN with high specificity and sensitivity
- "It was not possible to differentiate between a pre- and postsynaptic type of AS/AN in our collective."
Auditory Neuropathy Spectrum Disorder (ANSD): Audioligic Characteristics

- Hearing thresholds variable
  - From normal sensitivity through profound "hearing loss"
  - Rising audiogram configuration is common
- Absent ABR
- ECochG/ABR
  - Cochlear microphonic (CM) and summating potential (SP) present
  - Reversal of polarity of CM when recorded with condensation vs. rarefaction click signals
- OAEs present (often normal)
  - Lack of OAE suppression with noise (efferent abnormality)
- Fluctuating auditory status (may be temperature dependent)
- Poor temporal coding and processing
- Very poor word recognition scores, even in quiet
- Noise severely disrupts speech perception

ANSD: Audioligic Management

- Close monitoring until behavioral audiometry is complete
- Monitor OAEs
- Referral to other disciplines
- Hearing aids on trial basis with evidence of either:
  - Elevated pure tone or speech thresholds
  - Behavioral observation consistent with abnormal sensitivity
- Cochlear implantation as indicated
- FM technology
  - Personal FM system (e.g., Phonak iSense)
  - With Alternative communication strategies
  - Cued speech
  - Signing options (e.g., www.BabySigns.com)


<table>
<thead>
<tr>
<th>Risk factors reported for children with ANSD.</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity†</td>
<td>33</td>
<td>70.2</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>18</td>
<td>38.3</td>
</tr>
<tr>
<td>Jaundice</td>
<td>14</td>
<td>28.8</td>
</tr>
<tr>
<td>Exposure to certain drugs</td>
<td>3</td>
<td>6.2</td>
</tr>
<tr>
<td>Exchange transfusion</td>
<td>7</td>
<td>14.8</td>
</tr>
<tr>
<td>Family history of hearing loss</td>
<td>3</td>
<td>6.2</td>
</tr>
<tr>
<td>Birth trauma</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Central palsy</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Omeprazole exposure</td>
<td>2</td>
<td>4.3</td>
</tr>
<tr>
<td>Signs</td>
<td>2</td>
<td>4.3</td>
</tr>
</tbody>
</table>

†Defined as < 37 gestational weeks of birth.

<table>
<thead>
<tr>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 17 children with AN who received a CI</td>
</tr>
<tr>
<td>• Comparable control group with cochlear hearing loss</td>
</tr>
<tr>
<td>□ No significant difference between the groups on age of activation of the CI</td>
</tr>
<tr>
<td>□ Children with diagnosis of AN without associated cognitive or developmental disorders have speech and language outcomes comparable to other children who received a CI</td>
</tr>
</tbody>
</table>


| Children with ANSD experienced longer waiting period from diagnosis to hearing aid fitting and/or CI |
| □ Parents of children with ANSD reported significantly |
| • Different experiences of the diagnostic process |
| • Poorer understanding of the diagnosis |
| • Insufficient time allowed for asking questions |
| □ During the rehabilitation process |
| • 47% of parents with ANSD children reported receiving conflicting information |
| • Versus 0% of parents of SNHL children |

ANSID: Mulit-Disciplinary Management

| □ Otolaryngology |
| □ Ophthalmology |
| □ Neuroradiology |
| □ Developmental pediatrics |
| □ Neurology |
| □ Genetics |
| □ Speech language pathology |
| □ Others as indicated (e.g., Children’s Hospital with complete multi-disciplinary team) |

<table>
<thead>
<tr>
<th>Test</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>t</th>
<th>df</th>
<th>p</th>
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<tbody>
<tr>
<td>PLS-AC</td>
<td>365</td>
<td>1.9</td>
<td>40.5</td>
<td>2.6</td>
<td>11.9</td>
<td>52</td>
<td>0.1</td>
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<tr>
<td>PLS-BEC</td>
<td>361</td>
<td>1.7</td>
<td>39.4</td>
<td>2.5</td>
<td>11.8</td>
<td>52</td>
<td>0.1</td>
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<tr>
<td>PPVT</td>
<td>265</td>
<td>19.7</td>
<td>9.7</td>
<td>5.0</td>
<td>16.4</td>
<td>52</td>
<td>0.03</td>
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<tr>
<td>DEAP_C</td>
<td>265</td>
<td>5.1</td>
<td>3.8</td>
<td>6.3</td>
<td>2.1</td>
<td>52</td>
<td>0.07</td>
</tr>
<tr>
<td>DEAP_U</td>
<td>265</td>
<td>6.6</td>
<td>4.0</td>
<td>6.0</td>
<td>2.1</td>
<td>52</td>
<td>0.03</td>
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<tr>
<td>COQ</td>
<td>265</td>
<td>8.75</td>
<td>3.3</td>
<td>7.1</td>
<td>2.4</td>
<td>52</td>
<td>0.04</td>
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<tr>
<td>CROI</td>
<td>265</td>
<td>8.06</td>
<td>3.5</td>
<td>7.0</td>
<td>2.4</td>
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<tr>
<td>CTLD</td>
<td>265</td>
<td>8.35</td>
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<td>8.0</td>
<td>3.0</td>
<td>52</td>
<td>0.01</td>
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<tr>
<td>CELO</td>
<td>235</td>
<td>7.64</td>
<td>3.1</td>
<td>7.1</td>
<td>2.5</td>
<td>52</td>
<td>0.03</td>
</tr>
<tr>
<td>CLOQ</td>
<td>235</td>
<td>7.32</td>
<td>2.8</td>
<td>6.4</td>
<td>2.8</td>
<td>52</td>
<td>0.04</td>
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<tr>
<td>PEACH</td>
<td>230</td>
<td>7.11</td>
<td>2.8</td>
<td>7.0</td>
<td>2.2</td>
<td>52</td>
<td>0.08</td>
</tr>
</tbody>
</table>

- PLS = Preschool language scale
- PPVT = Peabody picture vocabulary test
- DEAP = Diagnostic evaluation of articulation and phonology
- PEACH = Parent’s evaluation of aural/oral performance of children

Thank You!
Questions?