Auditory Evoked Potentials: Mayo Clinic Audiology Conference

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ABR ancestry.....

• 43 years ago, today...
Audiology Test Battery

• The world of audiology in 1978:
  - ABR in its infancy
  - OAE’s yet to come
  - There was no IOM
  - Vestibular testing: mostly calorics, ocular pursuit, Barany chair (no posturography, sophisticated rotary chair)
  - Facial motility disorders: topognostic testing, i.e., taste, Schirmer’s

What do EP’s Tell Us?

• “Objective”, physiological tests:
  - Substitute for behavioral testing when developmental status (i.e., newborns, infants) or cognitive status (pathologic or drug-induced) do not allow for accurate behavioral responses
  - Supplement behavioral testing to better understand normal function, specific pathophysiology or specific auditory disorder
  - Neurodiagnostic/Diff.Dx. applications
  - Under the best circumstances, there is strong agreement between behavioral and physiologic tests
  - Need to understand the physiology of the test!
Clinical Impact of AEP’s

- The ultimate goal of performing clinical/diagnostic tests including AEP’s is:
  - To accelerate or improve treatment
  - To better understand normal function
  - To better understand underlying pathophysiology
  - Therefore we need to evaluate the contributions of different EP exams based on these principles

Questions

- Are we targeting a specific EP test appropriately to answer a specific clinical question
- Are we carrying EP tests that are redundant?
- Are we carrying out EP tests just because we can?
- Does the mere presence of a tracing or a graph provide relevant information?
- Is a given EP test sufficiently user friendly and informative to be appropriate for clinical use by the average clinician?
Is There a Role for ABR, Middle and Late AEP's Today?

- With appropriate test selection, and informed and skilled test administration and interpretation, auditory evoked potentials continue to be valuable clinical indicators of the functional status of the auditory system
  - Not with "shotgun" approach
  - Not in inexperienced hands
  - Not if using inappropriate equipment
  - Not with inappropriate technique
Objective measures of auditory function

- In 2008 we have an unprecedented menu of Auditory EP options for a wide variety of diagnostic applications, as well as unprecedented access to these EP through the availability of a wealth of equipment choices

Objective measures of auditory function: selective clinical applications

- Estimation of hearing sensitivity:
  - N1 (EcoG); EOAE*
  - ABR (wave V)
  - ASSR
  - MLR (esp. tone-bursts)
  - Late AEP (state-dependent, unreliable)
Objective measures of auditory function: selective clinical applications

- Neurodiagnostic applications:
  - **Cochlear Microphonic**: Auditory Neuropathy
  - **ABR** – CP-angle masses, intra-axial brainstem neoplasms, demyelinating disease;
  - **The Stacked ABR**: Don, Kwong and Tanaka
  - **MLR** – Central auditory dysfunction, primary auditory cortex
  - **BioMAP/BioMARK**: “BioMARK uses a speech syllable that reflects the acoustic characteristics of sounds that present difficulties for some individuals with reading and auditory processing disorders”.

Objective measures of auditory function: selective clinical applications

- Diagnosis of otological conditions:
  - **Electrocochleography**, SP/AP ratio
    - Endolymphatic Hydrops/Meniere’s Disease
    - Superior Semicircular Canal Dehiscence (SSCD)

- **Vestibular-Evoked Myogenic Potentials (VEMP)** – low threshold
  - SSCD

- **Central Processing**:
  - P300, MMN (oddball paradigm)
Threshold testing

Auditory EPs: Clinical Applications

• ABR:
  – Threshold testing with clicks and tone-bursts in newborns and infants in particular;
  – Increasing parallel applications in patients with cochlear implants;
  – Neurodiagnostic applications esp. in the elderly or in places where imaging studies are not readily available or rationed

AUDIOMETRIC THRESHOLDS
Means and Standard Deviations

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(49) (89) (48) (49) (45)
ABR click threshold v. 2-4KHz pure tones
500 Hz tone-pip ABR Threshold v. 500 Hz pure-tones

TIME
TRANSIENT
100 Hz STEADY STATE

FREQUENCY
100 Hz 0.2 µV
1000 Hz 10 µV
Carrier of 1 kHz
100% AM
25% FM
Modulation at 81 Hz

Activation at 1 kHz
Region of Basilar Membrane

Steady-State
Response at 81 Hz

Sound  Cochlea  Brain

Four stimuli presented simultaneously to one ear

Sound  Cochlea  Brain
MASTER - RESPONSE

- The scalp-recorded activity is converted into the frequency domain using a Fast Fourier transform (FFT) and the amplitude and phase of the response to each stimulus can be measured at the specific frequency at which the tone was modulated.

- The FFT data is presented as an amplitude spectrum of the averaged response.

The Auditory Steady State Response: Comparison with the ABR
Cone-Wesson et al.

TB ABR and ASSR thresholds were similar when both detected by automatic algorithm
Lowest thresholds obtained with visual detection/interpretation of ABR
ASSR advantage when thresholds in the profound range (Gary Rance)
Differential diagnostic/Neurodiagnostic Applications

- Cochlear Microphonic

- Auditory Brainstem Response

Infants With Auditory Neuropathy

- "Typical" test results:
  - Hearing loss
  - Complete absence of ABR including NI
  - Acoustic reflexes also absent
  - Cochlear microphonics present (outer hair cells)
  - Otoacoustic emissions present (outer hair cells)
  - ABR obtained with electrical stimulation present – suggesting that this may be a neural synchrony deficit
Demystifying the Cochlear Microphonic in AN

- **Myth:** cochlear microphonics (CM) are only present in patients with auditory neuropathy/dysynchrony (AN/D)
- **Reality:** CM is present in all patients/subjects with a reasonable complement of OHC if constant polarity stimuli are delivered
- In AN/D the CM is the only auditory potential present.
  - **Cochlear Microphonic-CM:** AC potential closely resembling the waveform of the acoustic stimulus related to synchronized variation in resistance of OHC during stimulation

Infants With Auditory Neuropathy: Implications For CI Candidacy

- The first important step in the rehabilitation of patients with AN is to confirm the hearing loss and its stability/dynamics
- Is auditory neuropathy a specific clinical entity? Actually, no: It is a configuration of test results suggesting a post-synaptic or neural etiology vs. a pre-synaptic, cochlear etiology but this result pattern does not specifically indicate site of lesion or pathophysiology.
- It is important to remember that the most relevant indication is some degree of hearing loss up to severe-profound.
Infants With Auditory Neuropathy:
Implications For CI Candidacy

- The clinical picture of AN including significant behavioral hearing loss may be transient: recovery of hearing including appearance of wave V of the ABR may occur over a 4-6-month period in patients with a diagnosis of prematurity, RDS and hyperbilirubinemia.
- Therefore, caution is advised when considering "AN patients" for cochlear implantation, in particular given the recent trend to implant by 6-month of age.

Case #1

- Diagnosed with severe to profound SNHL at 10 mos of age.
  - Absent ABR
  - Normal OAEs bilaterally
  - Referred for CI consideration at 2 years of age
  - Received CI at 2 ½ years of age
ABR

- Performed using clicks and 1000 Hz tone bursts
- Clicks: no wave V left ear at 95 dB, questionable wave V right ear at 95.
- Cochlear microphonics present in both ears for clicks and tone bursts.

EABR testing

- Positive response in each ear with intensities ranging from 600-800 microamps.
- Responses consisted primarily of a large wave III and a wave V, which was slightly more prominent for the RE.
Postop CI SF Audiogram
Inset: EAP's (NRT)

Device activated December, 2002
Good response to sound, programmed in 500 Hz ACE
Patient enrolled in AV therapy.
Parents report a noticeable increase in receptive vocabulary, increased vocalizations, and positive response to name.
AW: Hyperbilirubinemia

- Hyperbilirubinemia secondary to maternal-fetal ABO incompatibility.
- Diffuse mild symmetric T1 hyperintensity in globus pallidus, which likely relates to underlying hepatic failure.
- Passed initial screening prior to bilirubin elevation

AW: 35 weeks EGA, hyperbilirubinemia, 2 X transfusions
A: 2mos - inconsistent responses to loud sounds;  B: 6mos - SF 20-25 dB
AW: 35 weeks EGA, hyperbilirubinemia, 2 X transfusions

Audio, 24 mos

- 2 mos: responds inconsistently to loud sounds
- 13 weeks: starts babbling
- 16 weeks: SF SDT 35 dB
- 7 mos: SF 20-25 dB across freq. range; ABR present
- 11 mos: 5 words, flat tymps
- (PE tubes age 14 mos.)
- 24 mos: SF 10-20 dB across freq. range

AW, age 4 yrs.
Audiology Test Battery

- Retrocochlear pathology: Differential Diagnosis
  - ABLB
  - SISI
  - TONE-DECAY
  - REFLEX DECAY
  - ABR
  - OAE
  - IMAGING: MRI WITH GADOLINIUM

Audiology Test Battery

- We are doing far less neurodx. ABR's than 10-15 years ago, why?
  - Imaging technology
  - Several publications indicating the low sensitivity of the ABR in identifying small tumors (60%+) - - this is due in most cases to poor technical quality, and lack of adjusting test methodology to hearing loss pattern
Bad ABR !!

Audiology Test Battery

- MRI: "gold standard", but also depends on technical quality and experience of interpreter
  - Considered to have a sensitivity of 100% for CPA masses of 2-3mm<
  - Does the audiologist still have a role in contributing to the Dx of CPA masses?
Audiology Test Battery

• THE ABR
  – SENSITIVITY: 90% + (bad rep in dx of small, 1cm>AN)
  – Technical quality important for interpretation
  – Experience of interpreter also important as is the ability to make on-line decisions during test administration

ABR Protocol

• Insert earphones
• Clicks, 85 dBNHL
• 1KHz tone pips
• Two-channel montage
• Parameters measured:
  – Waveform morphology
  – Absolute and interpeak latencies
Hierarchy of Differential Diagnosis with the ABR

- Establish presence or complete absence of ABR – interpret relative to hearing status of test ear
- If ABR present, determine if gross response morphology is normal or not: absence of wave V is abnormal; absence of wave I may relate to cochlear hearing loss
- If gross morphology normal, measure interpeak latencies relative to norms
ABR Interpeak Latency Criteria

- I-III > 2.3 ms
- III-V > 2.1 ms
- I-V > 4.4 ms
- ILD V > 0.40 ms
- For 1KHz tone-pips (Blackman function), ILD V > 0.60 ms
  - Wave V latency > 6.85 ms (7.75 ms)

Normal ipsilateral ABR – Interwave Intervals
ABR Interpretation for Retrocochlear Screening

- Using an effective stimulus level, is the ABR present?
- If present, is the response morphology grossly normal (backtrack from V)?
- If "yes" to the above, are interpeak and/or absolute latencies wnl?

Right Acoustic Neuroma
El-Kashlan, Eisenmann and Kileny
Ear and Hearing, 2000

- 25 patients with AN, 1cm>
- 23/25 abnormal ABR(92%)
- 3/23 – complete absence of ABR in spite of PTA 23-50 dB
- 20/23 – abnormal I-III and/or I-V IPL
- 15/20 – abnormal ILD - V

The Derived-band Technique

Click stimuli are delivered in the presence of high-pass masking noise. The cutoff frequency of the high-pass noise is lowered from one run to the next. This process masks progressively lower frequency areas of the cochlea. Subtracting the response for one run from the previous one forms a derived-band response. Here, the response to clicks + 8 kH high-pass masking noise is subtracted from the response to clicks alone to form the derived-band ABR with center frequency (CF) = 11.3
The Stacking Method

Derived-band ABR
- Neural contributions from different frequency regions of the cochlea can be obtained using the derived-band ABR method.
- Derived-band ABRs represent activity from more specific frequency regions than moderate-to-high level toneburst-evoked ABRs.

Stacked ABR
- The Stacked ABR is formed by temporally aligning wave V of the derived-band ABRs and then summing the responses.
- Aligning the derived-band ABRs eliminates phase cancellation of lower frequency activity. Thus, the Stacked ABR amplitude reflects activity from all frequency regions of the cochlea, not just the high frequencies.
- Reduction of any neural activity due to a tumor, even a small tumor, will result in a reduction of the Stacked ABR amplitude.

Uluru Sunset
EcoG: Novel Applications

Superior Canal Dehiscence (SSCD)

- Auditory manifestations
  - Hyperacusis to bone conducted sounds, autophony
  - Audiometry: air-bone gap, intact acoustic reflexes

- Vestibular manifestations
  - Sound and pressure-evoked vestibular symptoms
  - Lower VEMP thresholds

- Our observation: patients with SSCD have abnormal electrocochleography (ECoG)
Subjects

- 11 patients with auditory ± vestibular manifestations of SSCD
- SSCD confirmed by CT in 15 ears
  - Unilateral: 7 patients
  - Bilateral: 4 patients

Audiometric Findings

Frequency (Hz)

Air-bone gap (dB)
VEMP Testing

- VEMP threshold (dB)  Mean ± SD
  Affected ears  67 ± 10
  Unaffected ears  82 ± 5

- VEMP thresholds were ≤ 65dB in 13/15 affected ears

Electrocochleography

- Measurement of sound-evoked inner ear electrical potentials

- Summating potential (SP)
  - Sum of individual hair cell potentials

- Action potential (AP)
  - Sum of auditory nerve fiber action potentials

- Increased SP is associated Meniere’s disease
EcoG: placing TM electrode

EcoG: final setup with insert phone
Electrocochleography (ECoG)

- ECoG performed in standard fashion
- Stimuli
  - Alternating polarity clicks
  - Intensity 85dBrHL
- SP/AP > 0.4 defined as abnormal

ECoG Results

- 15 affected ears
  - 14 ears
  - 1 ear
  - Mean ± SD
    - 0.40 ± 0.29
- 5 unaffected ears
  - Mean= 0.27; SD=0.14
  - 1 ear
    - 0.65

*(thin ipsilateral SSC, contralateral SSCD)*
Postoperative Results

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<th>Post-op SP/AP</th>
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Pt 1. Pre-op and post-op ECoG

Intraoperative ECoG

- Immediately after canal occlusion:
  - SP decreased
  - AP increased (slightly)
  → SP/AP normalized

- SP/AP remained stable post-op (0.32)
Summary

- SP/AP was elevated in 14/15 ears & had a borderline value in 1/15 ears with SSCD
- SP/AP normalized after canal occlusion

Implications

- SSCD should be added to the differential diagnosis of an elevated SP
- SP elevation may vary less in SSCD than in Meniere’s disease patients
- SSCD may be used as a model system
  - Origin of summating potential
  - Pathophysiology of endolymphatic hydrops
Mechanism of SP elevation in SSCD

- Displacement of the basilar membrane toward the scala tympani results in SP elevation (in animal models)

- "3rd window" may alter hydrodynamic forces \(\rightarrow\) basilar membrane bias

Mechanisms

- Rosowski et al., 2004: as a result of the dehiscence, impedance may be larger on scala vestibuli side than scala tympani side at certain frequencies. This may result in a BM bias towards scala tympani and a resultant increase in SP.
Acknowledgements

- H. Alexander Arts, MD
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- Greg Mannarelli, AuD
- Bruce M. Edwards, AuD

Proof of principle: Canal Occlusion

- Right posterior semicircular canal occlusion procedure for refractory benign paroxysmal positional vertigo
- Ecog monitored
- SP/AP increased when canal opened in preparation for occlusion
- SP/AP normalized with canal occlusion, and remained spable
Cognitive EP's; Central Processing

P300

- Requires the ability to distinguish differences between stimuli
- Requires and "oddball" paradigm whereby a series of identical stimuli (frequent) are interspersed by the occasional stimulus that differs in some regard (rare or target)
- Usually a task associated with the identification of the target stimuli is assigned, but response can also be obtained with passive listening.
- Typical ratio is 80/20%, and a total of 30-100 stimuli presented at a slow rate are sufficient
AVERAGED ENCEPHALIC RESPONSE OF APHASICS TO LINGUISTIC AND NONLINGUISTIC AUDITORY STIMULI

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PAMELA J. MERTING
Hearing and Speech Center of Rochester, Rochester, New York

Oddball Paradigm
P300

- P3A: elicited by large stimulus differences whether the subject is attending or not.
- P3B: Subject needs to actively attend to the target stimuli
- P3 is usually best recorded from central, midline, slightly parietal electrode locations
- May be elicited by a variety of stimuli and contrasts, including “missing” stimuli
P300 Principles

Parallel processing: attention-driven working memory change (frontal lobe, P3A) and temporal-parietal lobe activation from memory updating operations (P3B)

![Diagram showing the process of P300 principles]

P300: early clinical applications

Middle Latency (MLR) and Late Vertex Auditory Evoked Responses (LVAER) in Central Auditory Dysfunction

Paul Kleinv, Ph.D.
P300: test-retest

Test-Retest Variability of Auditory Event-Related Potentials

Paul A. Allman, and Andra Reiter Uppal

Division of Audiology, Department of Otolaryngology, Head and Neck Surgery, University of Michigan Medical Center, Ann Arbor, Michigan

Figure A: Test-retest variability of auditory ERPs (P300) across two test sessions. Each subject participated in both test sessions, and the data were analyzed using paired t-tests.

Figure B: Scatterplot showing the relationship between P300 latency and subject age. The latency is plotted against subject age, with different colors representing different test sessions.

P-300 latency as a function of age: Frequent-800 Hz, Rare-1000 Hz
Low-resolution Electromagnetic Tomography (LORETA)

A functional brain imaging method that estimates the current density (electric neuronal activity) distribution in a 3D Talairach space (Pascual-Marqui et al., 1994, 1999).

Tonal Task

NH (12)

Right CI (6)

Left CI (3)
Changes in the time course and patterns of brain activation during the initial period post-implantation: preliminary data

- AERP recordings at 4, 10, & 16 weeks post-initial stimulation
- 3 post-lingual adults (2 females)
- Mean Age: 52.5 y
- Duration of deafness: 20.3 y
- Nucleus 24C (ESPrint; ACE)
- Implant side: right

Behavioral Measures
Vowel Height Discrimination Task

Performance Accuracy

Reaction Time
Event-related Potentials


Henkin, Kileny,Hildesheimer,and Kishon- Rabin
ERP study

- An investigation of the effects of increasing acoustic-phonetic difficulty in children with cochlear implants
- Vowel place, vowel height, voicing, place of articulation
- ERP measures: P300 latency and amplitude
- Behavioral measure: accuracy in identifying target (oddball paradigm) and reaction time

ERP study

- P3 latency and reaction time increased with increasing difficulty
- P3 amplitude and performance accuracy decreased with increasing difficulty
- Speech perception performance relates to neurophysiological responses at cortical level
BioMAP/BioMARK

- From Nina Kraus' Lab at NWU

- A “different” kind of auditory perception indicator
Brain Stem Response to Speech: A Biological Marker of Auditory Processing

Krista L. Johnson, Trent G. Nicol, and Nina Kraus