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Neurodiagnostic Auditory Evoked Response Applications

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Agenda

I. Background and introduction; clinical utility of MLR and CERP in neurodiagnosis
II. Review of stimulus and recording parameters for MLR
III. MLR analysis and interpretation
IV. Review of stimulus and recording parameters for MLR
V. CERP analysis and interpretation
VI. Summary, Q & A

Background and Introduction

In Current Clinical Practice

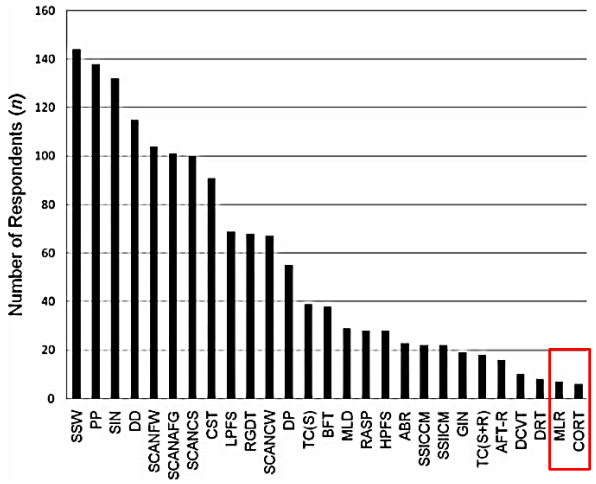
- Widespread
  - Click and Toneburst ABR
- Not as Widespread
  - ECochG
  - ASSR
  - MLR
  - LLR
  - P300

Table 5 Administration of Electrophysiologic Tests (n = 212)

Test	*%*
Evoked otoacoustic emissions	33
Electrocochleography	25
Auditory brainstem response	65
Middle latency responses	9
Late evoked responses	2
40-Hz potential	1
Mismatch negativity (MMN)	1
Cognitive (P-300) response	5
Electronystagmography	47
Other	7
Do not test	25

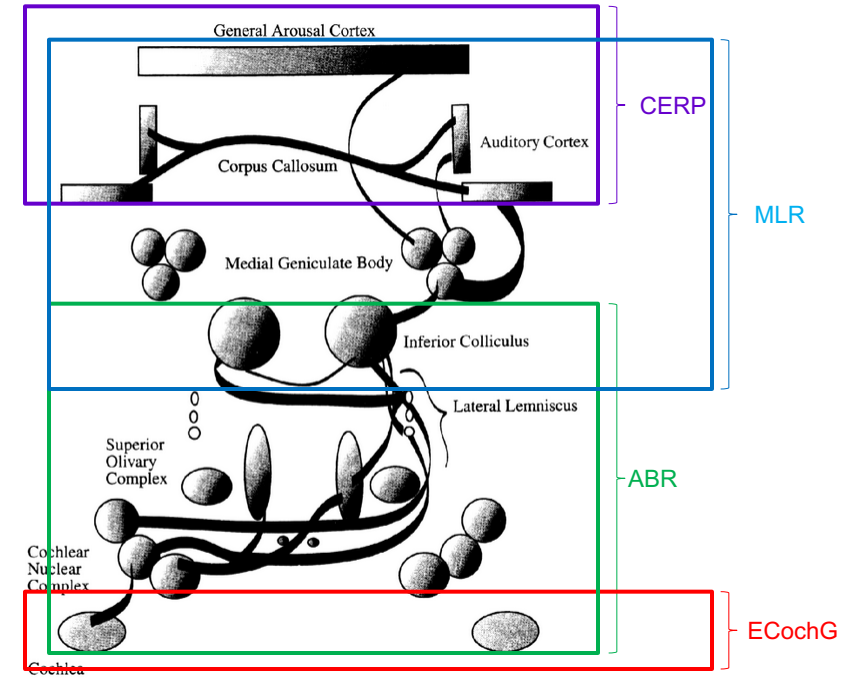
N = 212

Martin et al (1998); JAAA



N = 195

Emanuel et al (2011); AJA

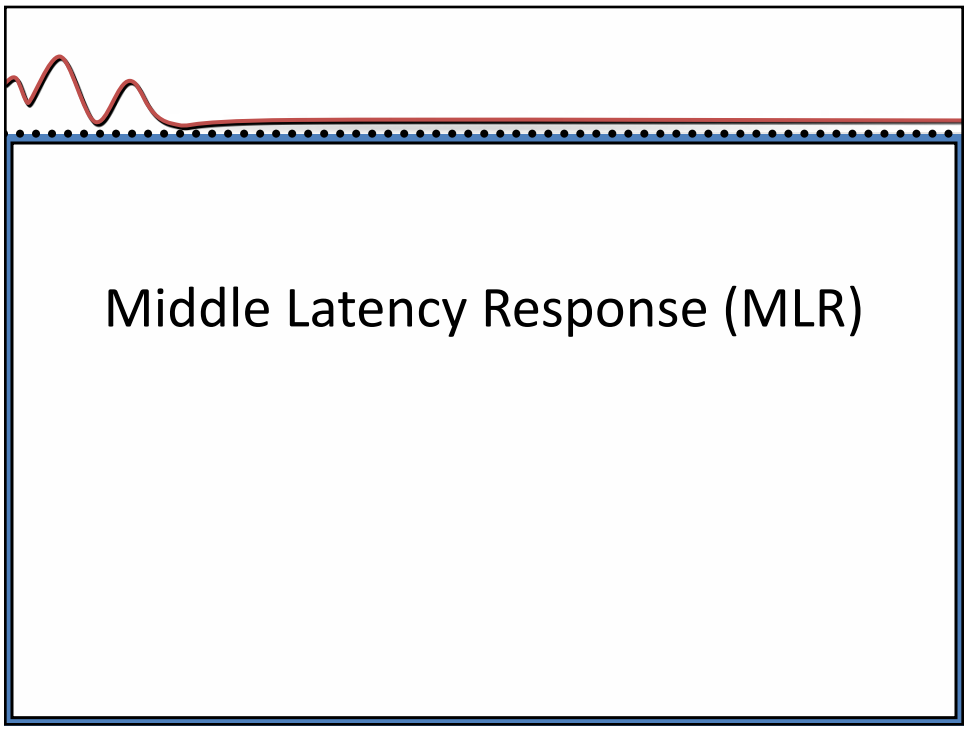


With Permission from Herbert Jay Gould, Ph.D. (in Atcherson & Shoemaker, 2012)

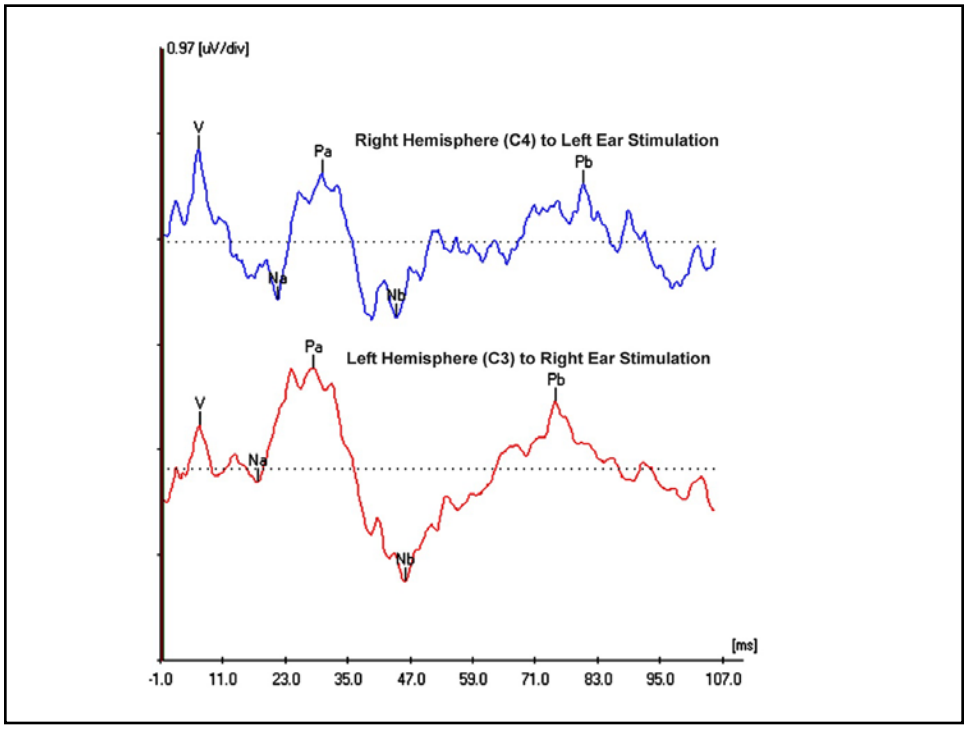
WYSINWYG

- Except for Wave I, no 1-to-1 relationship between peaks/valleys and auditory structures
  - Assumptions*:
    - Valleys = cell body activity (stationary sources)
    - Peaks = traveling action potential activity (moving sources)
    - Straight or bending pathways
    - Changes in conduction medium
    - Multiple generators beyond cochlear nucleus
- Parallel and crossed pathways
- Open and closed fields
- Changes from *action potentials* to *post-synaptic potentials* as we advance to the cortex

*See Moore (1987); Moller (1994); Eggermont (2007); Picton (2011)

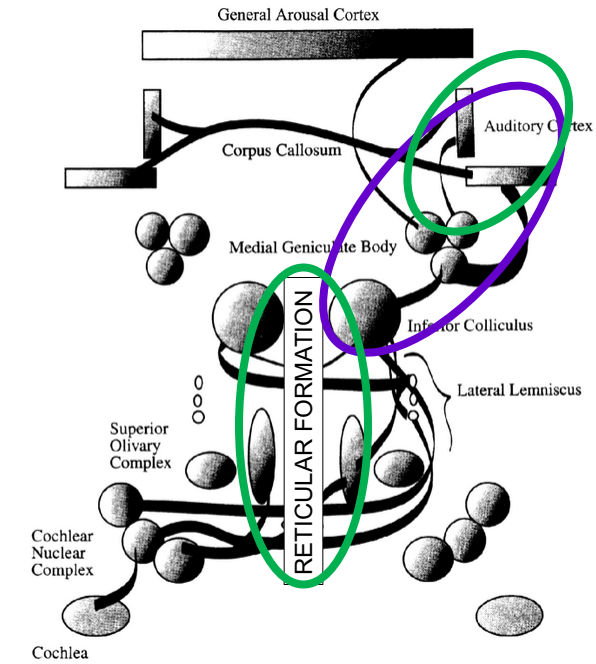


Middle Latency Response (MLR)



MLR

- Characteristics
  - Several vertex positive and negative peaks
    - Na – approximately 18 ms (2nd most robust wave)
    - Pa – approximately 30 ms (most robust wave)
    - Pb – approximately 50 ms (also referred to as P1 of the cortical potentials)
    - Also others: No, Po, Nb, Nc, and Pc



Pa

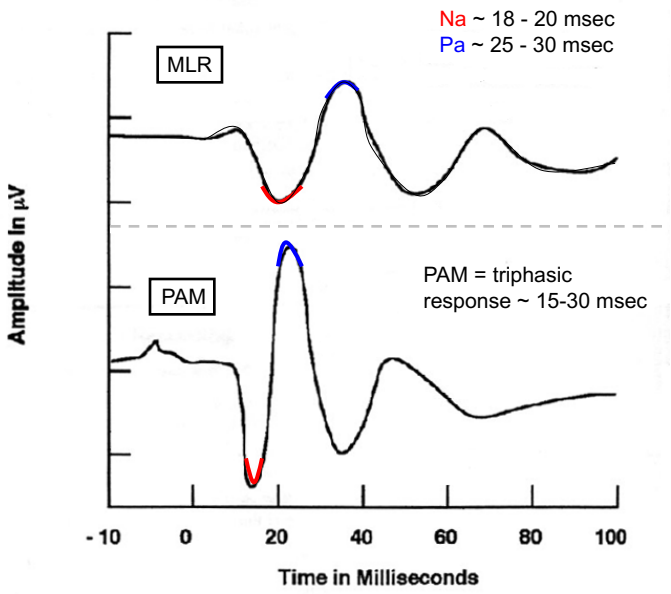
Na

With Permission from Herbert Jay Gould, Ph.D. (in Atcherson & Shoemaker, 2012)

Sonomotor Responses

- Acoustic stimuli can activate muscles
- Examples Encountered in Audiology
  - Stapedius M.
  - Sternocleidomastoid M.
  - Inferior Oblique M.
  - Post-Auricular M.

MLR and PAM artifact share same time domain:

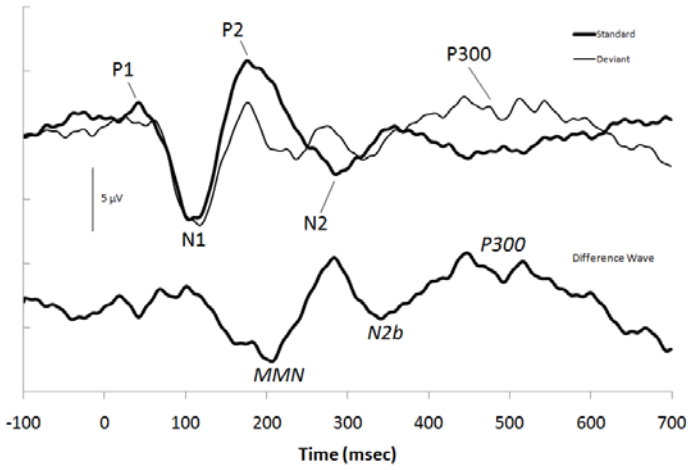


Cortical Event-Related Potentials (CERP)

First Things First on CERPs

- Names: cortical auditory evoked potentials (CAEP), late auditory evoked potentials (LAEP), late auditory response (LAR), late-latency response (LLR); cortical event-related potential (CERP)
  - For this presentation, I use CERP to describe the family, but will use LLR and P300
- Both exogenous and endogenous components (some more than others)
- Patient state needs to be awake and alert

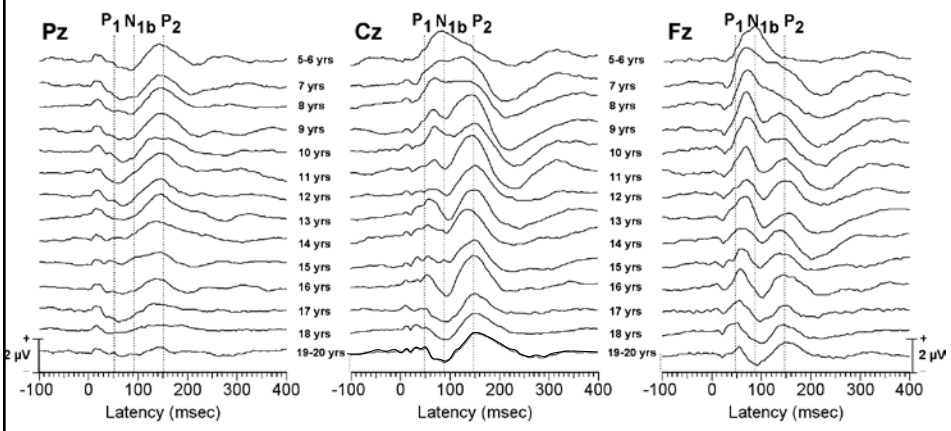
Family of CERPs

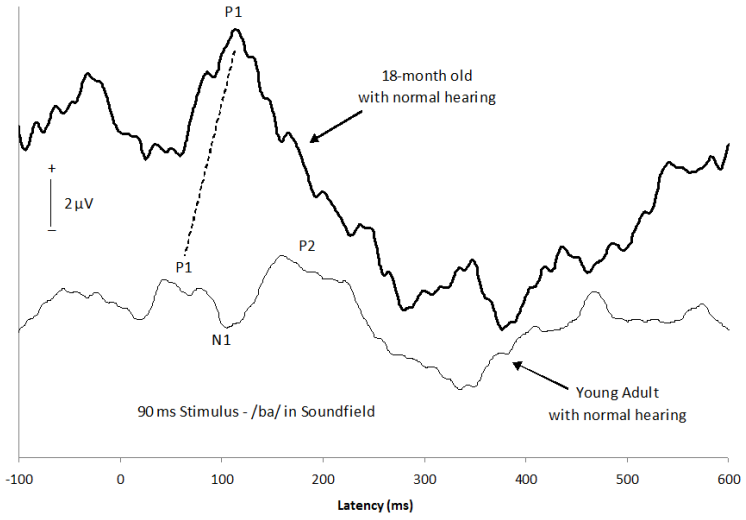


LLR

- Occur between 50 and 250 ms (generally cannot see MLR and earlier waves)
- All "classic" components are obligatory
  - P1 (aka Pb or P50)
  - N1 (approximately 100 ms)
  - P2 (approximately ~180 ms, seen as early as 150 ms)
- Generators
  - Typically the auditory and association cortex, but not solely
  - May be influenced by reticular activating system and frontal cortex

Ponton et al. (2002)





White & Atcherson (2011)

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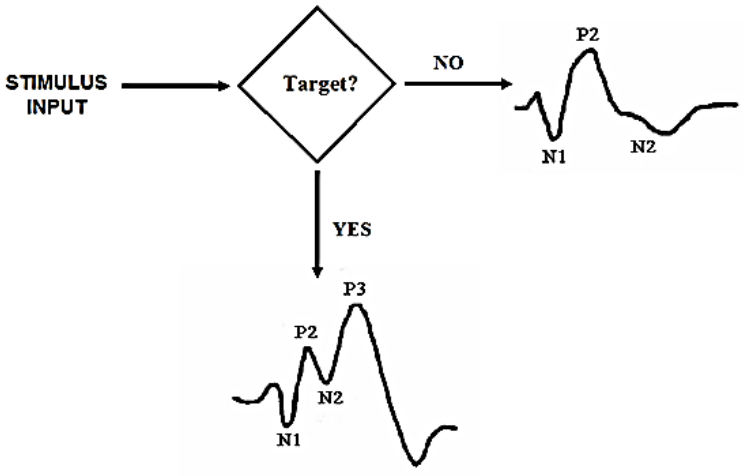
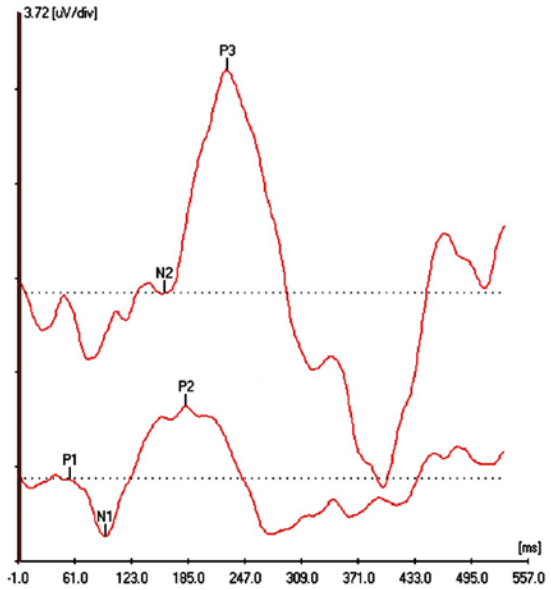
P300

- Occurs between 250 and 600 msec
- Multiple cortical and subcortical sites, including thalamus and reticular formation
- Can be elicited by variety of sensory stimuli
- A “cognitive” response based on subject’s attention during an oddball paradigm
- Appears to reflect “timing” of cognitive processes

Standard versus Target



In Prout (2005), adapted from Polich (2003)

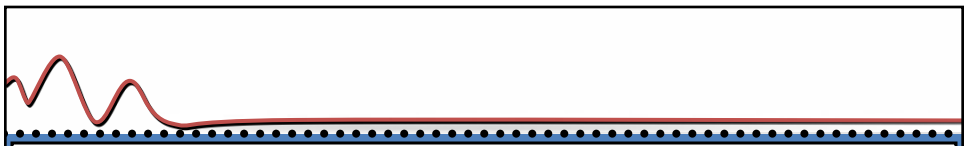


Average to 2000 Hz
(Target; Infrequent)

Average to 1000 Hz
(Standard; Frequent)

P3a versus P3b versus Novelty

- P3a – shorter latency evoked during passive oddball paradigms (deviant ignored)
- P3b – longer latency evoked during task-oriented oddball paradigms (deviant attended to)
- Novelty – similar in latency to non-target stimuli (because subject is not looking for it)



MLR Stimulus and Recording Parameters

Test Protocol for MLR

Parameter	Recommendation	Comments
Transducer	ER-3A Inserts	TDH-49 will work too
Mode	Monaural	
Stimulus Type	100 µsec Click, < 10 msec tone burst	Clicks are most commonly used for neurodiagnosis
Rate	7.1 to 17.1/sec	Slower may enhance later components
Intensity	70 dB nHL	Higher may elicit PAMR
Sweeps	500 to 1000	

Test Protocol for MLR

Parameter	Recommendation	Comments
Time Window	80 to 100 msec	Short pre-stimulus may be useful
Amplification	50,000 to 75,000x	
Artifact Rejection	±30 to 50 µV	
Notch Filter	Off	
Filter Settings	0.1 to 300 Hz 10 to 300 Hz 10 to 3000 Hz	MLR Only + Pb MLR Only MLR + some ABR
Ocular Channel	See comment	Not required, but may be helpful
Replication	Minimum of 2 runs	May be helpful to average replicated runs for analysis

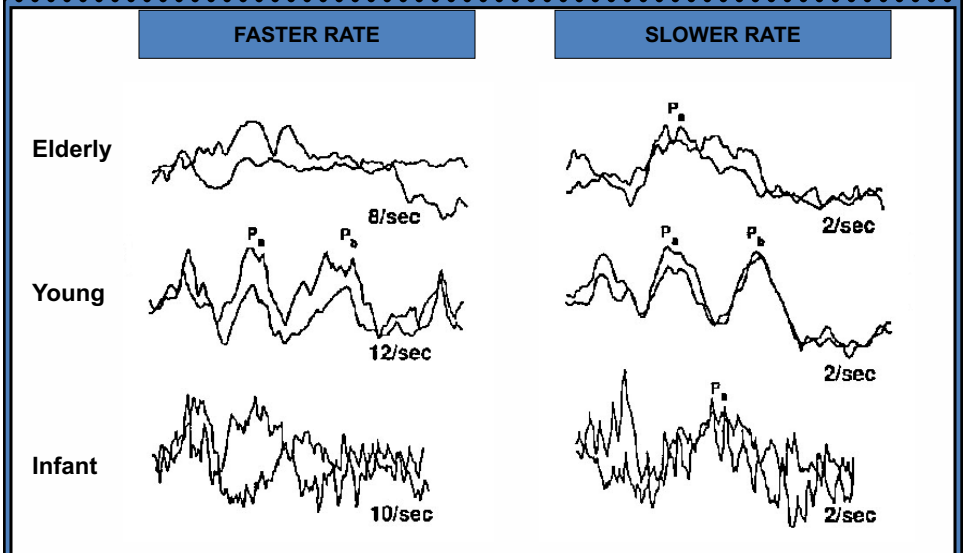
Electrode Montage

- Montage:
  - (+) Non-inverting (active) at Cz plus C5/C6 or C4/C3
  - (-) Inverting (reference) on earlobe/mastoid (e.g., A1 and A2)
  - Ground (depends on the montage, if single channel – earlobe, if multi-channel - Fpz)
- Placement of reference electrode important due to muscle artifact issue
- Selection of reference site will influence results
  - Non cephalic site?
  - Linked earlobes?

Active Electrode Sites

- Placement of electrodes aids in site of lesion testing
- Symmetric bilateral representation
  - Used for neurodiagnosis in locating hemispheric differences
  - Use multiple electrode sites to look for electrode/ear effects
    - e.g., C4-A1, C3-A1, C4-A2, C3-A2,… C4-A1, C3-A2

Effect of Rate and Age



Effect of Stimulation Rate

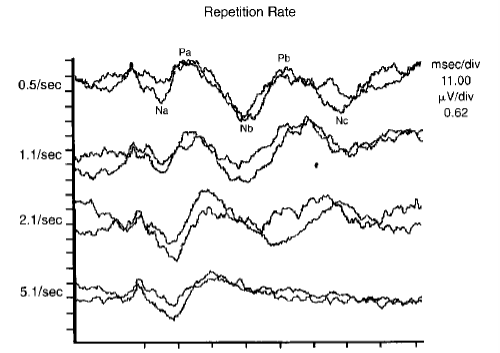


Figure 4 An example of AMLR waveforms as a function of rate for adult subject JW. As the stimulus rate increased, the amplitude of Pb decreased. The stimulus was a 500-Hz tone burst with a duration of 60 msec. The noninverting electrode was located at Fz and the inverting electrode at NC.

Nelson, Hall, & Jacobson, 1997

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Effect of Patient State

- MLR is reliably recorded in awake subjects, and those in light sleep (stage 1 and REM)
- Subjects do not have to 'attend' to stimuli
- Amplitudes are greatly reduced in heavy sleep and heavy sedation, especially in infants and children

MLR Analysis and Interpretation

Waveform Analysis

- Typically measure latency and/or amplitude of various peaks
- Amplitude more important for MLR than latency
  - Less precise latency resolution due to less high frequency information and smaller sample sizes (sampling rate vs. window size)
  - Latency difference of 1-2 msec for MLR is considered negligible

Clinical Applications of MLR

- Central lesions
- Auditory processing disorders
  - Hemispheric study
- Differential diagnosis (ABR, MLR, and LLR)

Site of Lesion Testing

- Cases where MLR potentials are preserved in presence of severe-profound thresholds
  - Cortical deafness diagnosis (Woods et al, 1987)
- Some cases may show normal ABR wave V but abnormal Pa response (Kileny et al., 1987)
  - Differential diagnosis is important!

Site of Lesion Testing

- Ear effects vs Electrode Effects
- Ear effect: responses reduced/absent at all electrode sites for a given stimulus ear, but not for other ear
- Electrode effect: responses reduced/absent at given electrode site regardless of ear stimulated

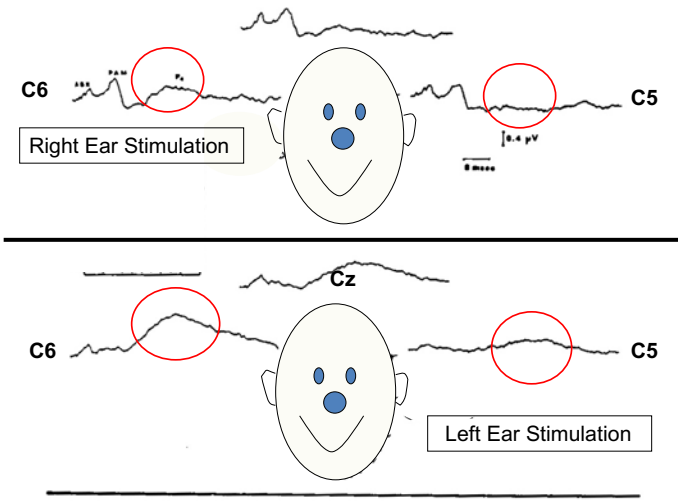
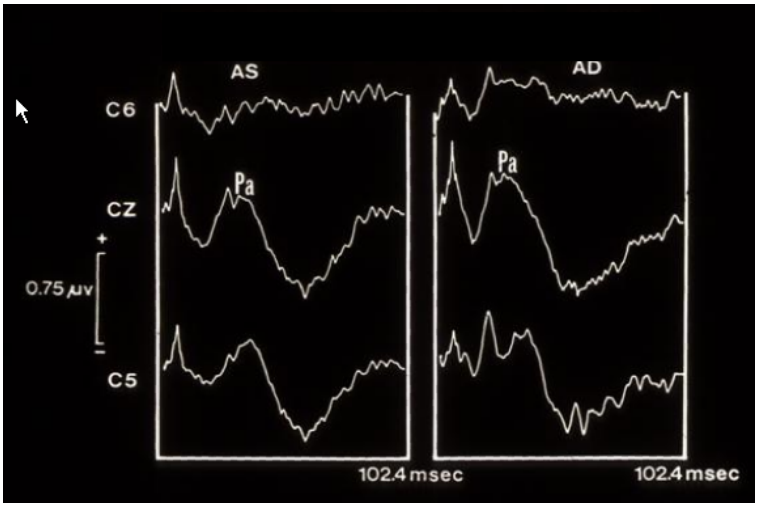


FIGURE 7.4. Coronal distribution of wave Pa in a patient with a left temporo-parietal lesion and severe Wernicke's aphasia. Pa was largest over the intact hemisphere as compared to the vertex, and absent over the lesioned side, regardless of the ear stimulated. The patient's pure tone audiogram is shown on the left. "PAM" refers to posterior auricular muscle activity. (Reprinted with permission from Kraus, Özdamar, Hier,and Stein, *Electroencephalography and Clinical Neurophysiology, 54*, 275–287, 1982).

Kileny et al. 1987



Ear effect or Electrode effect?

Purdy et al. (2002)

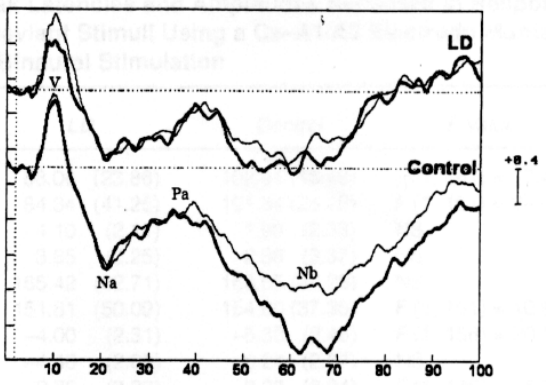


Figure 3 Grand-averaged right ear (*thick line*) and left ear (*thin line*) middle latency response waveforms recorded using Cz–Cv2 electrode montage. Responses of the learning-disabled (LD) and control children are shown at the top and bottom, respectively.

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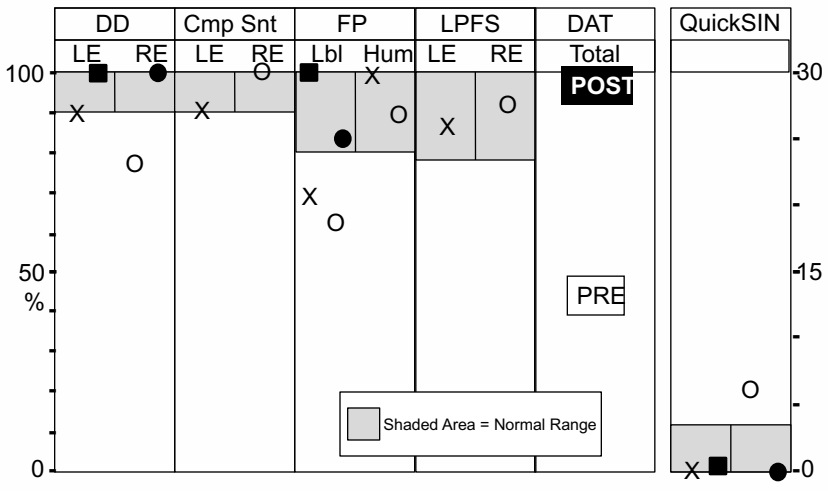
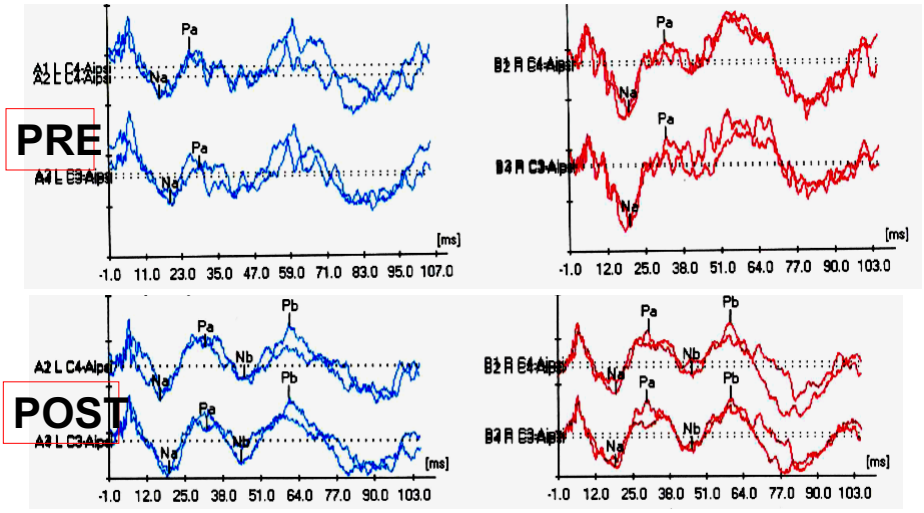
Hemispheric Asymmetry

- When the amplitude of MLR is 50% or more on one hemisphere to contralateral stimulation compared to the other hemisphere with contralateral stimulation, this is construed as a positive finding. Lesion? Possibly… (after Musiek et al., 1999)
- An ear effect may be more likely than electrode effect in APD (Schochat et al., 2004)

Dichotic Auditory Training



Pre- and Post-Training MLRs



Pratt (2007)

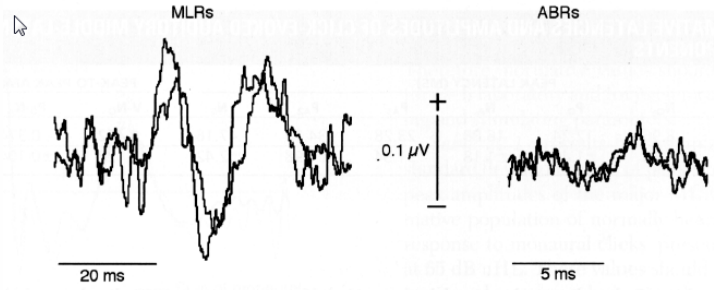


FIGURE 22.7. MLRs from an adult patient with impaired speech perception and discrimination, incompatible with his audiogram, which showed only a mild low-frequency hearing loss. His cochlear function was preserved, as evidenced by normal cochlear microphonic potentials in response to 1 kHz tone bursts (not shown). Only a very low amplitude peak V could be detected in his brainstem potentials (ABR), far worse than expected from his audiometric findings. The clearly recorded MLRs, in contrast to the nearly absent ABRs, are compatible with the diagnosis of Auditory Neuropathy.

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Jerger & Jerger (1985)

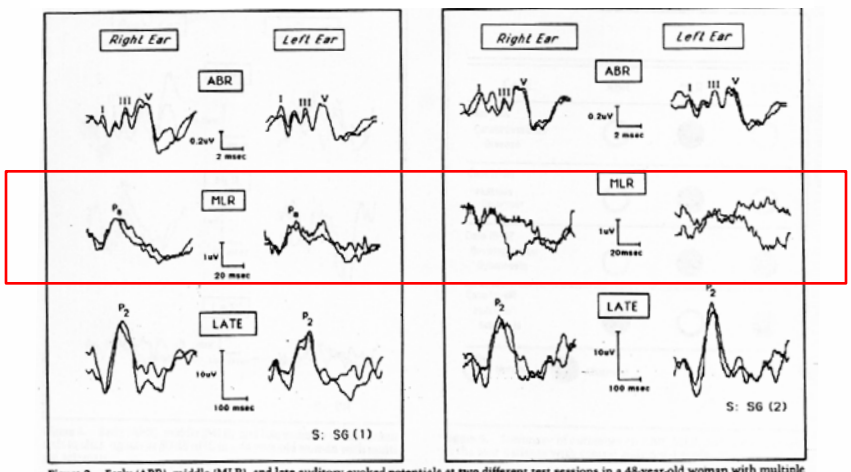

Figure 2. Early (ABR), middle (MLR), and late auditory evoked potentials at two different test sessions in a 48-year-old woman with multiple sclerosis. Test signals were click trains (ABR) or 500-Hz tone bursts (MLR and late) at 70-dB nHL. **Figure 2a** (at left) S:SG (1): First evaluation; **Figure 2b** (at right) S:SG (2): Reevaluation five months later.

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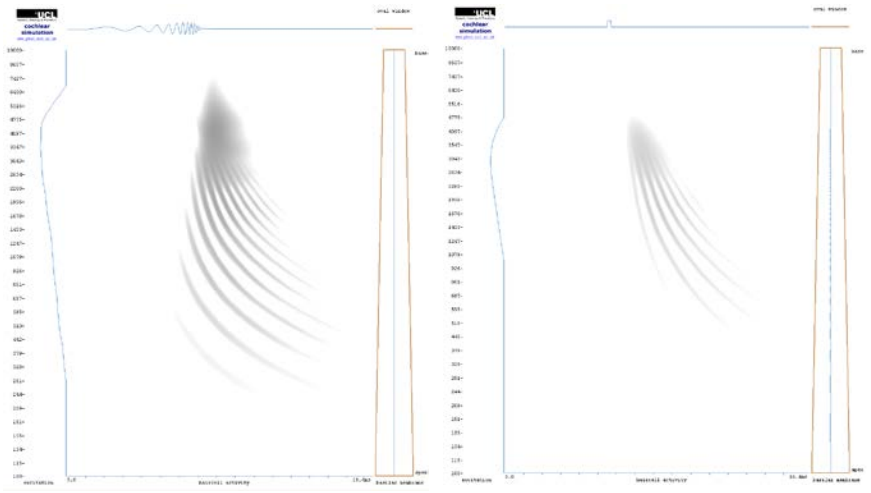
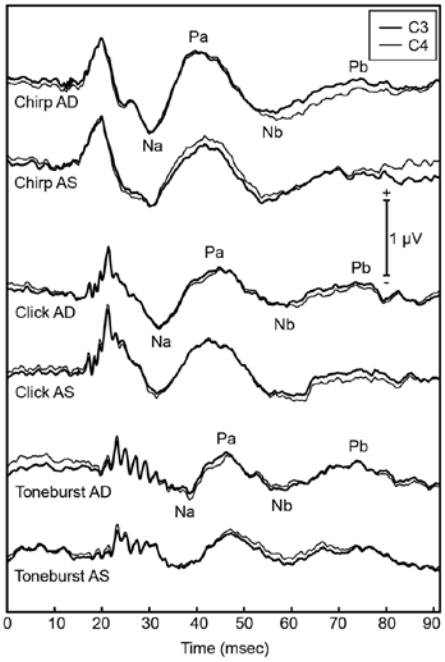


Created using: http://www.phon.ucl.ac.uk/resource/cochsim/

Is there any benefit of the input compensation chirp for MLR? In other words, does MLR benefit from increased neural synchrony?

Atcherson & Moore
(under revision with
J Am Acad Audiol)



CERP Stimulus and Recording Parameters

Test Protocol for LLR

Parameter	Recommendation	Comments
Transducer	ER-3A Inserts	TDH-49 will work too
Mode	Monaural	
Stimulus Type	100 µsec Click, ~50 msec tone burst, Speech stimuli	Depends on purpose of LLR
Rate	0.7 to 1.7/sec	High rates attenuate
Intensity	70 dB nHL	Higher may elicit PAMR
Sweeps	200 to 500	Few as 50; as much as 1000

Test Protocol for LLR

Parameter	Recommendation	Comments
Time Window	500 msec	Add -100 msec pre-stimulus
Amplification	50,000x	
Artifact Rejection	±100 µV	
Notch Filter	Off	
Filter Settings	0.1 to 100 Hz 1 to 30 or 40 Hz	Online filtering Offline filtering
Ocular Channel	Yes	At least one above or below 1 eye
Replication	Minimum of 2 runs	May be helpful to average replicated runs for analysis

LLR Electrode Montage

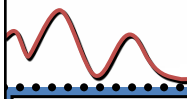
- Montage:
  - (+)Non-inverting (active) at Cz or Fz
  - (-) Inverting (reference) at earlobe(s) or mastoid(s)
  - Ground (depends on the montage, if single channel – earlobe/mastoid, if multi-channel Fpz)
  - Ocular electrodes for eyeblink detection/rejection
- Make sure not on PAM if mastoid is used
- Selection of reference site will influence results
  - Non cephalic site? Nape of Neck
  - Linked earlobes? Not always recommended

Test Protocol for P300

Parameter	Recommendation	Comments
Transducer	ER-3A Inserts	TDH-49 will work too
Mode	Monaural	
Stimulus Type	~50 msec tone burst (1000 and 2000 Hz), Speech stimuli (CVs)	Which is standard/frequent; which is target/infrequent
Rate	0.7 to 1.7/sec	Sometimes less may be needed
Intensity	60 dB nHL	Audible; verify calibration
Sweeps	200 to 500	Few as 50; as much as 1000

Test Protocol for P300

Parameter	Recommendation	Comments
Time Window	500 msec	Add -100 msec pre-stimulus
Amplification	50,000x	
Artifact Rejection	±100 µV	
Notch Filter	Off	
Filter Settings	0.1 to 100 Hz 1 to 30 or 40 Hz	Online filtering Offline filtering
Ocular Channel	Yes	At least one above or below 1 eye
Replication	Minimum of 2 runs	May be helpful to average replicated runs for analysis



P300 Electrode Montage

- Montage:
  - (+)Non-inverting (active) at Cz or Fz or Pz (or all three)
  - (-) Inverting (reference) at earlobe(s) or mastoid(s)
  - Ground (depends on the montage, if single channel – earlobe/mastoid, if multi-channel Fpz)
  - Ocular electrodes for eyeblink detection/rejection
- Make sure not on PAM if mastoid is used
- Selection of reference site will influence results
  - Linked earlobes? Not always recommended

CERP Analysis and Interpretation

CERP Clinical Applications*

- Cortical lesions
- Auditory processing deficits
- ANSD
- Audibility/ Verification

* Many potential uses for CERP, but still under active research

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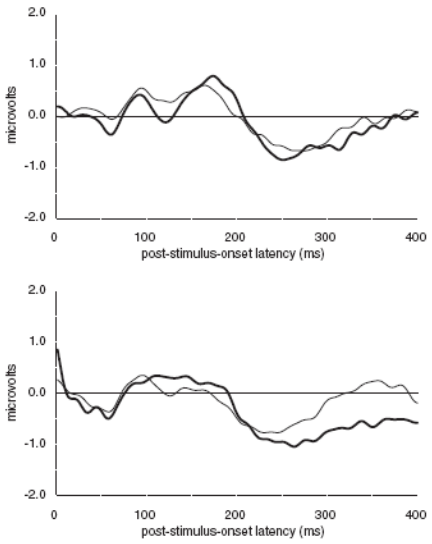
Auditory Processing Deficits in Language/ Learning Problems

Wible et al. (2005)

4-/da/ stimuli with 361 ms ISI

Co-presented in Noise

Thick line: normal
Thin line: LP



First /da/

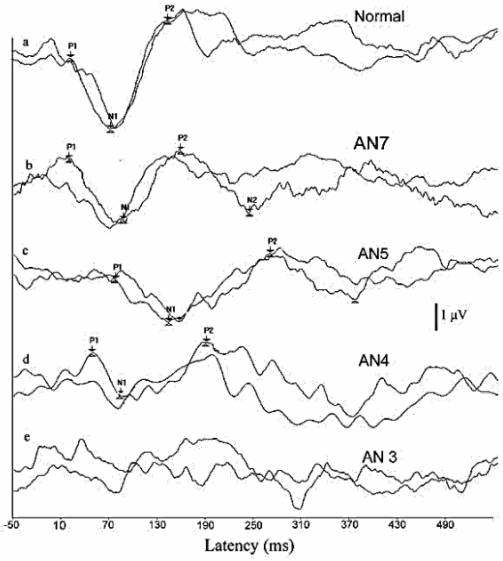
Fourth /da/

Testing in Absence of ABR

Narne & Vanaja (2008)

The better the speech perception, the better the morphology of cortical response

AN = auditory neuropathy



Jerger & Jerger (1985)

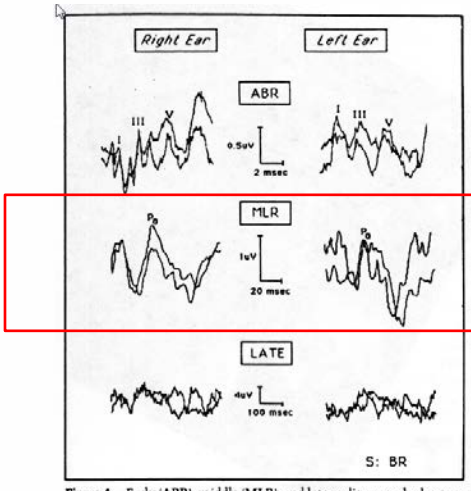


Figure 4. Early (ABR), middle (MLR), and late auditory evoked potentials to click signals at 80-dB nHL in a 44-year-old woman with multiple sclerosis.

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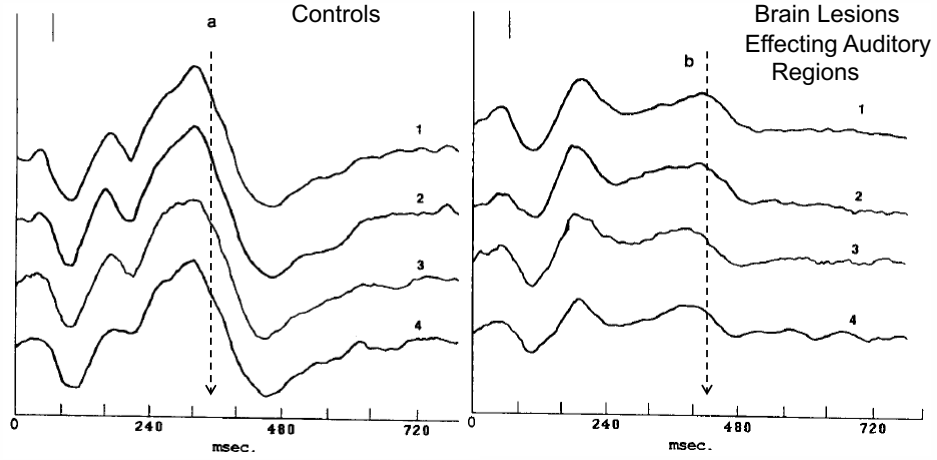
Audiology Example of P300



1 = C3/left ear, 2 = C4-right ear, 3 = C4/right ear, 4 = C3/left ear

Musiek et al. (1992)

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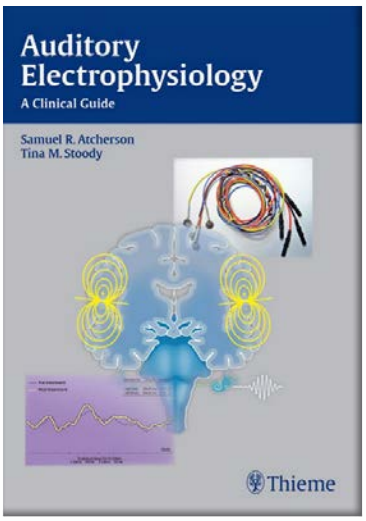
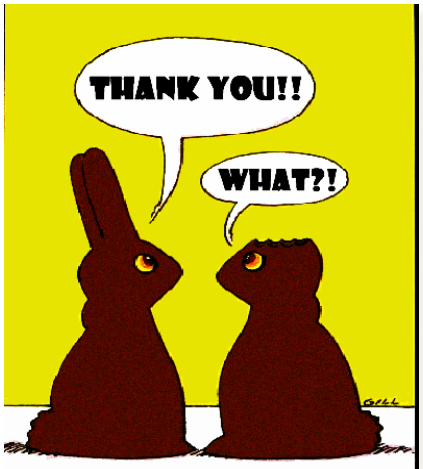
Summary

- Most commercial systems (at the very least) will allow you to record LLR
- Lots of potential clinical uses for LLR, but more research is required
- Most exciting is testing for Auditory Processing Deficits in various disorders, and Cortical Testing for Hearing Aids and Cochlear Implants
- Stay Tuned…with the literature

Questions?





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AudiologyOnline Tech Support: 800.753.2160

Update on Auditory Electrophysiology: Evidence-Based Clinical Applications

Application of ABR in Objective Assessment of Infant Hearing
James W. Hall III, PhD

Clinical Applications of Electrocochleography in Audiology Today
James W. Hall III, PhD

Neurodiagnostic Auditory Evoked Responses Applications
Samuel R. Atcherson, PhD

Cortical Response Applications for Audiometric and Audibility Assessment
Samuel R. Atcherson, PhD

www.audiologyonline.com/electrophys2013