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- I have **relevant financial relationship(s)** with the products or services described, reviewed, evaluated, or compared in this presentation.
 - NIH-NIDCD and AUCD
 - ✦ Grant recipient to conduct research.
 - James Madison University
 - ✦ Honorarium paid for the 2013 Ruth Symposium in Audiology and Hearing Science.
- I have no relevant nonfinancial relationship(s) to disclose.

Innovations in the Electrophysiologic Assessment of Infant Hearing



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PH.D.**

**THIS RESEARCH WAS SUPPORTED BY A
GRANT TO BARBARA CONE BY
ASSOCIATION OF UNIVERSITY CENTERS
ON DISABILITY (AUCD). RTOI-2010-03.**

Long Term Goals of Research



- Apply knowledge of auditory system function and development to provide
 - Cost-effective
 - Sensitive
 - Specific
 - Efficient
- tools for infant auditory assessment.

Why these goals?



- Electrophysiologic methods must be used to determine hearing sensitivity in the first few months of life.
 - Ear and frequency specific estimates of hearing threshold are crucial to EHDI planning.
 - Electrophysiologic test results are usually the sole indicator of an infant's hearing levels until the infant is developmentally and motorically able to provide a behavioral response.
 - ✦ 6-9 months of age for typically developing infants, later for those with developmental delays.

The Auditory Brainstem Response



- The auditory brainstem response has been used for infant assessment for the past 35 years.
- Threshold estimates from ABR tests are used to fit hearing aids when behavioral testing is not possible.

The Problem



- The ABR is a very small “brain wave” compared to the electrical energy produced by the brain.
- Interference from muscle movement (even blinking or swallowing) can compromise the ability to get valid threshold estimates.
- It is usually necessary to have the infant sedated for a full diagnostic ABR test to be completed.

Costs of Sedated ABR



- There are high costs associated with sedated ABR:
 - Expense of administering sedative (nurse or nurse/anesthetist)
 - Expense of monitoring state of the infant
 - Risk of respiratory and/or cardiac distress and failure
 - Risk of undiagnosed hearing loss (with cascade of poor outcomes) when parents opt out of testing due to fear regarding the procedure.

Improving the ABR test



- Question:
- Are there methods or technologies that could be used that would significantly decrease test duration so that evaluations could be completed during
 - brief periods of quiet sleep
 - Quiet wakefulness
- Such methods/technologies would need to
 - Reduce the effects of infant movement on ABR
 - Improve the amplitude of the response relative to the noise from infant movement.

Innovations



- Three methods were evaluated as “Innovations in the Electrophysiologic Assessment of Infant Hearing”, research supported by the Association of University Centers on Disability (AUCD).
- 1) Advanced signal processing as implemented on the Vivosonic Integrity ABR System
- 2) New stimulus: “Chirp”
- 3) New response paradigm: cortical evoked steady-state response.

Vivosonic Integrity





What's different about Vivosonic?



Innovation

- A Kalman (adaptive) filter
- An in-situ amplifier
- Blue-tooth communication for data transfer

Benefit

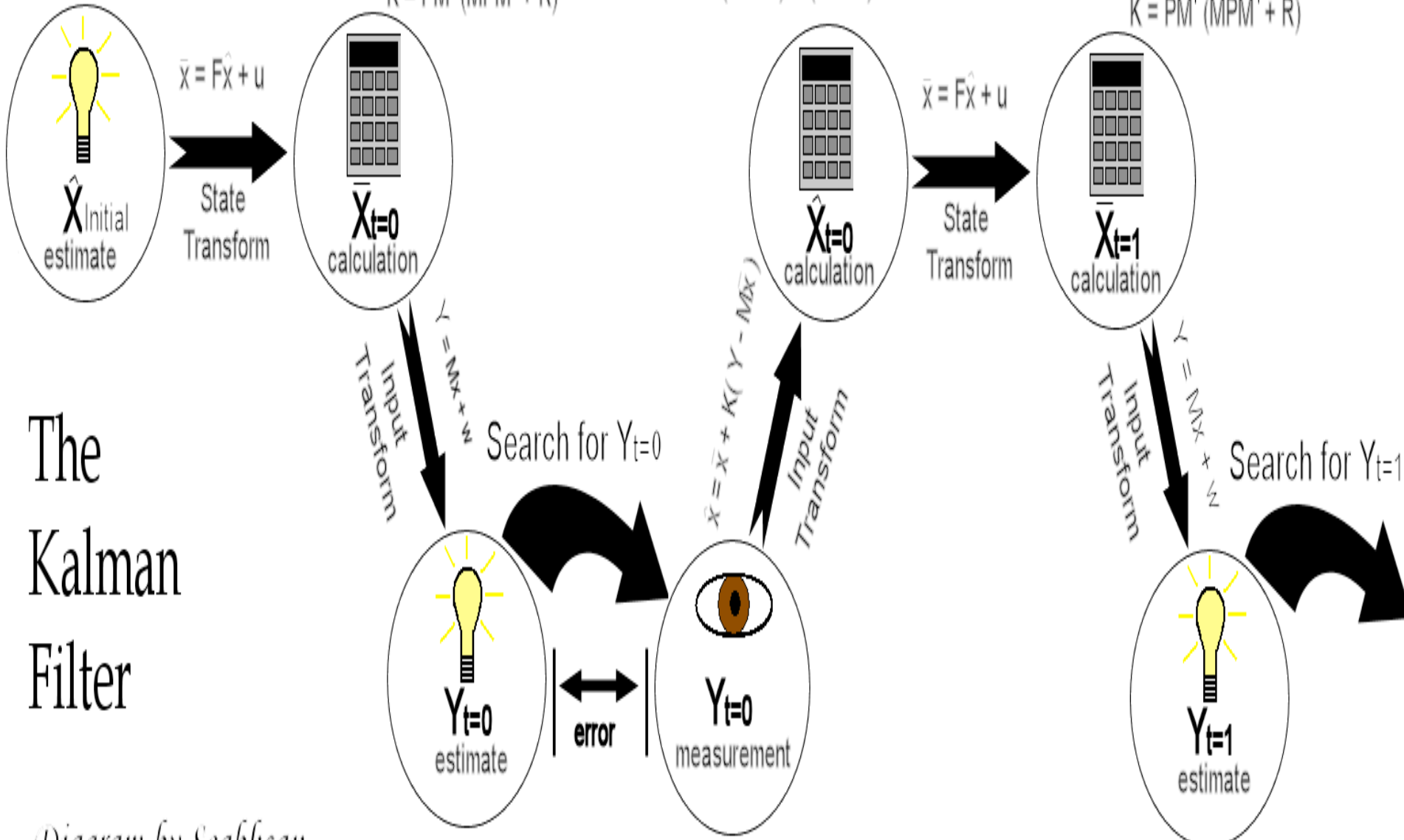
- “smart” filter, adapts to noise conditions and weights data appropriately for averaging.
- “Amplitrode”- combined electrode and amplifier.
- Patient is not tied to the computer. Parent can rock or walk around with baby during data acquisition.

Update P (Error Cov Matrix)
 $P = (I - KM) \bar{P} (I - KM)^T + KRK^T$

Project P ahead
 $\bar{P} = FPF^T + Q$
 Update K (gain)
 $K = \bar{P}M^T (M\bar{P}M^T + R)^{-1}$

Update P (Error Cov Matrix)
 $P = (I - KM) \bar{P} (I - KM)^T + KRK^T$

Project P ahead
 $\bar{P} = FPF^T + Q$
 Update K (gain)
 $K = \bar{P}M^T (M\bar{P}M^T + R)^{-1}$



The Kalman Filter

Diagram by Seabfican

The Kalman filter is an algorithm that uses a series of measurements observed over time, containing noise (random variations) and other inaccuracies, **and produces estimates of unknown variables** that tend to be **more precise than those based on a single measurement alone**

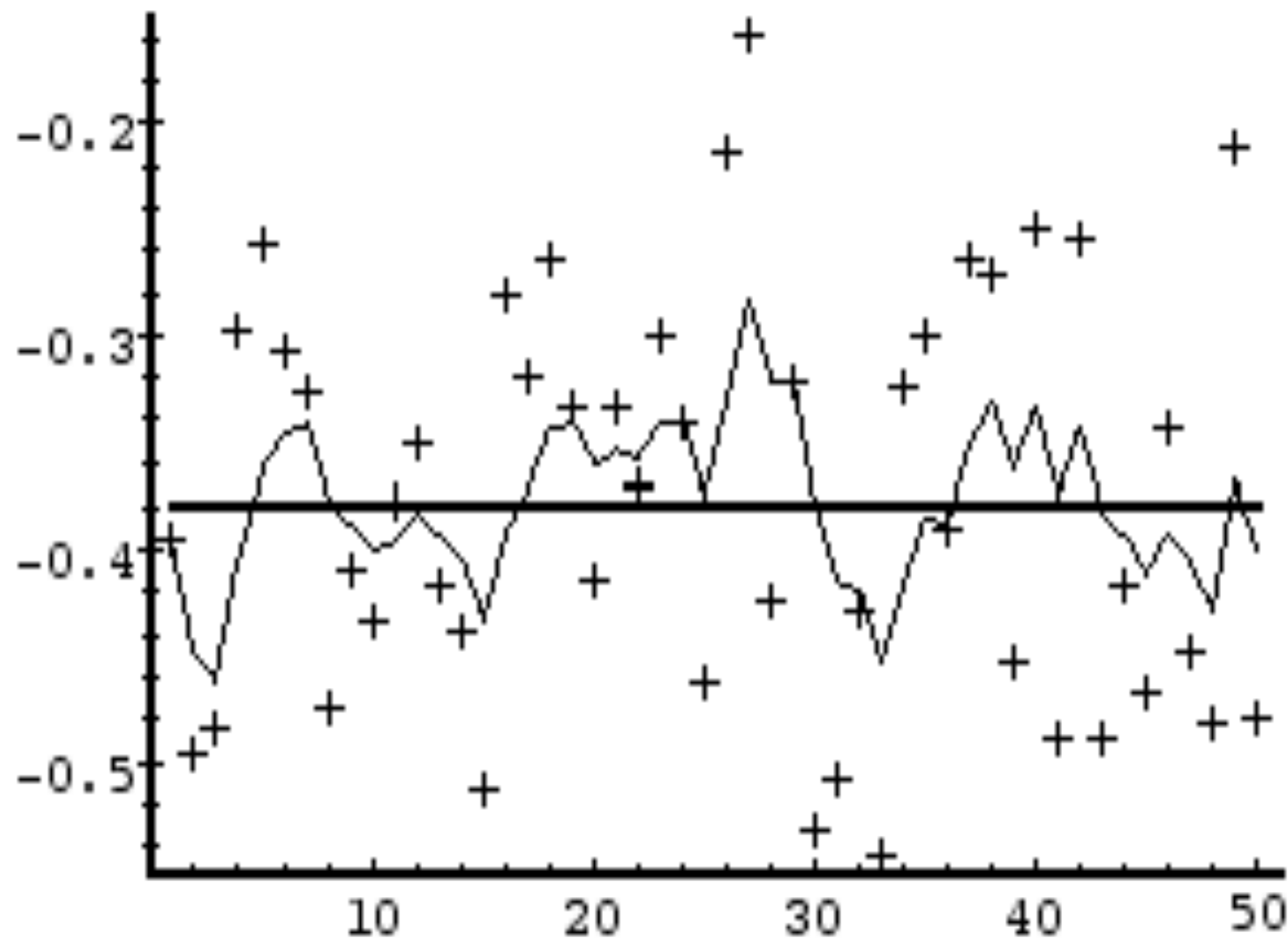
The Kalman filter has numerous applications in technology. The Kalman filter is a widely applied concept used in signal processing.

The algorithm works in a two-step process:

Prediction: the Kalman filter produces estimates of the current state variables, along with their uncertainties.

Updating: estimates are updated using a **weighted average**, with more weight being given to estimates with higher certainty.

Voltage



Response-to-Noise Ratio



- In conventional ABR tests,
 - EEG amplification,
 - averaging, and
 - amplitude-based artifact rejection
- are used to improve the ABR-to- noise ratio.

- Use of a Kalman filter has potential of reducing ABR averaging time by 75% compared to conventional methods (Chan et al 1975).

Experiment 1: Independent Verification



- Our first experiment was designed to determine if there was a difference in the ABR latency and amplitude when obtained using "experimental" (Vivosonic) technology, compared to conventional technology.
- Normally hearing adults were tested in 3 conditions:
 - Quiet, relaxation
 - Reading aloud
 - Making random motor movements
- The threshold, latency and amplitude of the ABR were evaluated as a function of recording method and listening condition.

Experiment 2: Clinical Verification



- The “experimental” system that employed the kalman-filter was used in a clinical setting.
- The audiologist using the system was not asked to vary her test protocol in any way, except for initiating ABR measurements while the infant was still awake.
- The presence and latencies of the ABR responses obtained during wakefulness were measured.
- The number of sweeps, needed to obtain a waveform was quantified.

Experiment I Methods

Independent Verification



- **40 normally hearing young adults**
- **Stimulus:** 100 μ s click presented at a rate of 27.7/s
- Cz-A2 electrode montage, A1 ground for conventional (control) recording performed with an Intelligent Hearing systems Smart-EP system
- Fpz-A2 electrode montage, Fp ground for experimental (Vivosonic) recording, according to manufacturers recommendation

Acquisition Parameters



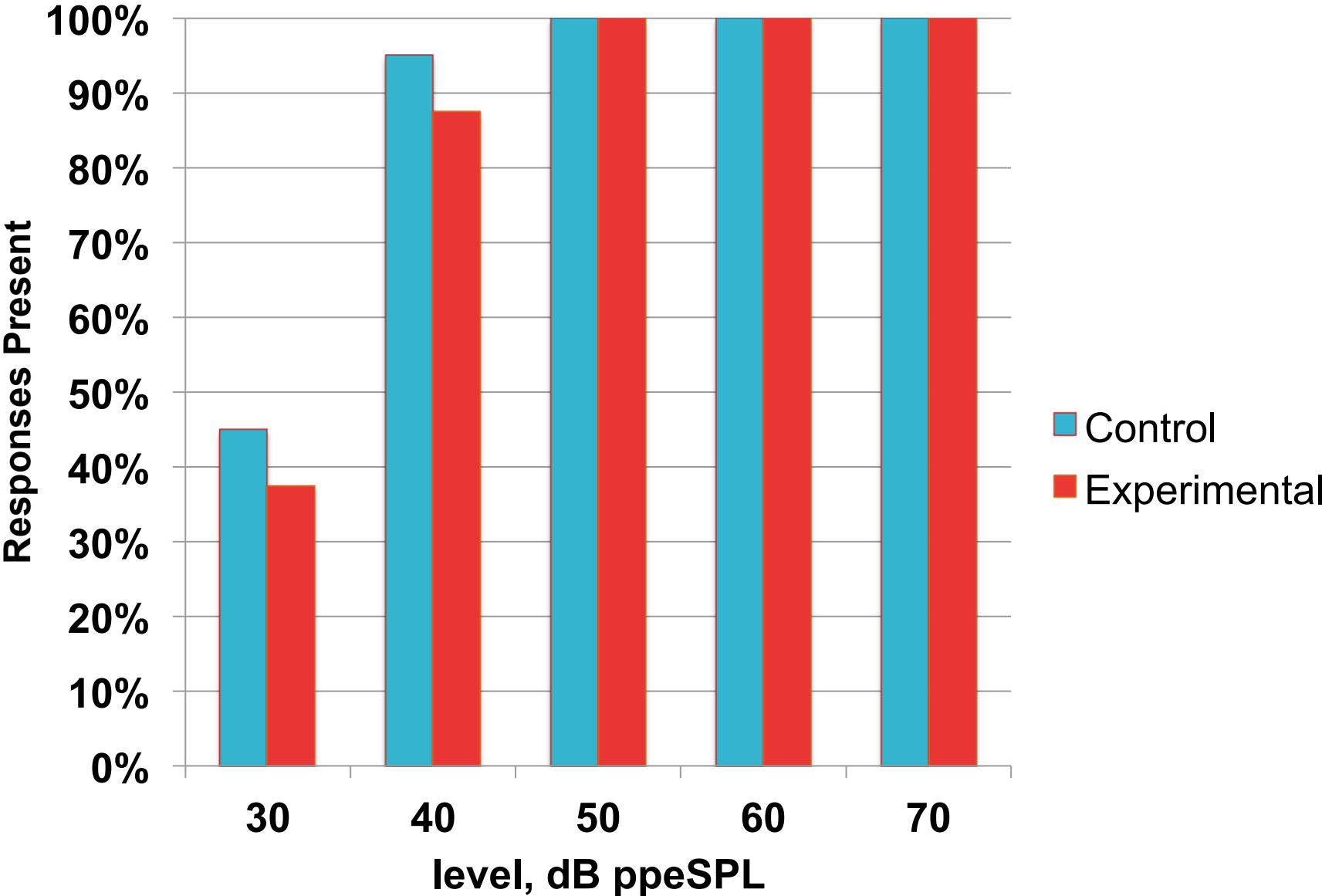
- EEG filter at 100-3000 Hz for both instruments.
- Amplitude based artifact reject level set at 20% for conventional (control) recording.
- Kalman filter as implemented in Vivosonic Integrity ABR system for "experimental" system.

Procedure

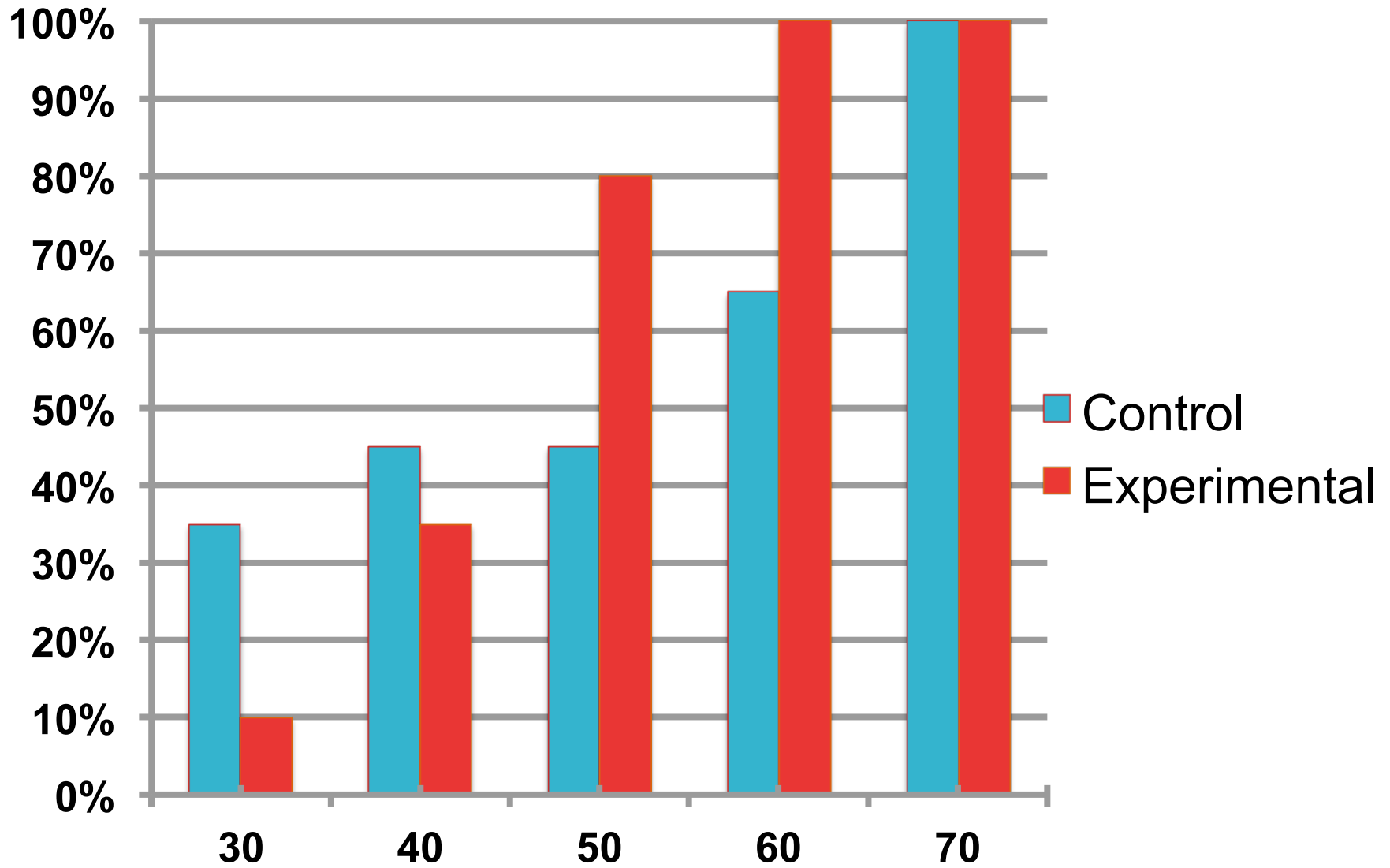


- 3 test conditions were performed for each subject using both instruments with order of device randomized across subjects
- **Quiet condition:** ABRs were obtained at each 10 dB decrement from 90 dB ppeSPL until no response was evident. 2000 sweeps were averaged for each trial and responses were replicated at each level.
- **Steady state noise condition.** Subjects read aloud from a magazine while ABR recordings were obtained. Test levels were at 70 dB ppeSPL and decremented in 10 dB and then 5 dB steps as threshold was approached. Each waveform was recorded for 3 minutes. The lowest level at which a response was obtained was replicated.
- **Intermittent noise condition.** ABR traces were recorded while the subject performed motor tasks on cue (i.e. humming, writing in the air, or naming objects) every 30 seconds. Starting at 50 dB ppeSPL, ABRs were averaged for three minutes at each 10 or 5 dB decrement as threshold was approached. The lowest level at which a response was obtained was replicated.

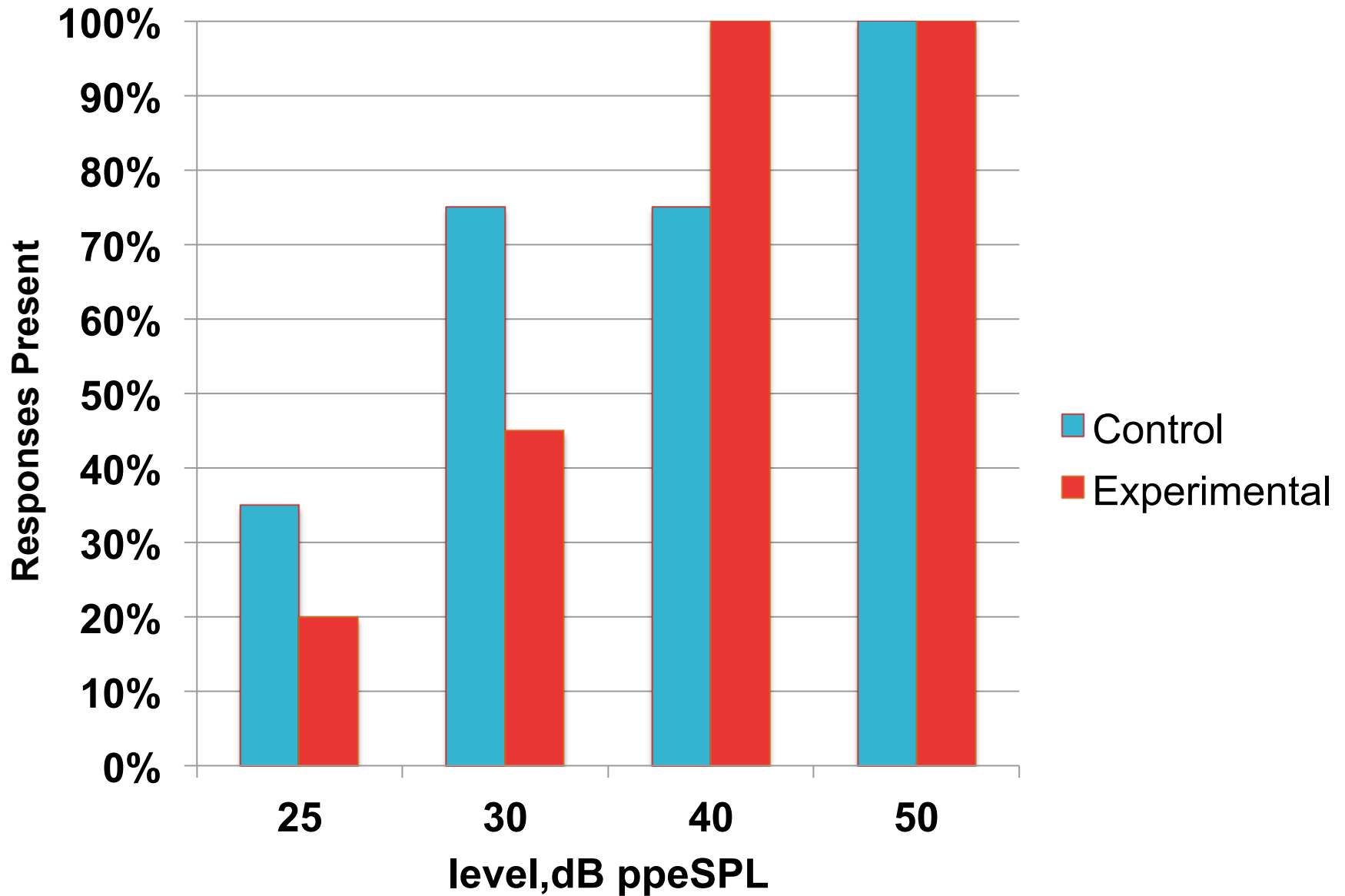
Quiet

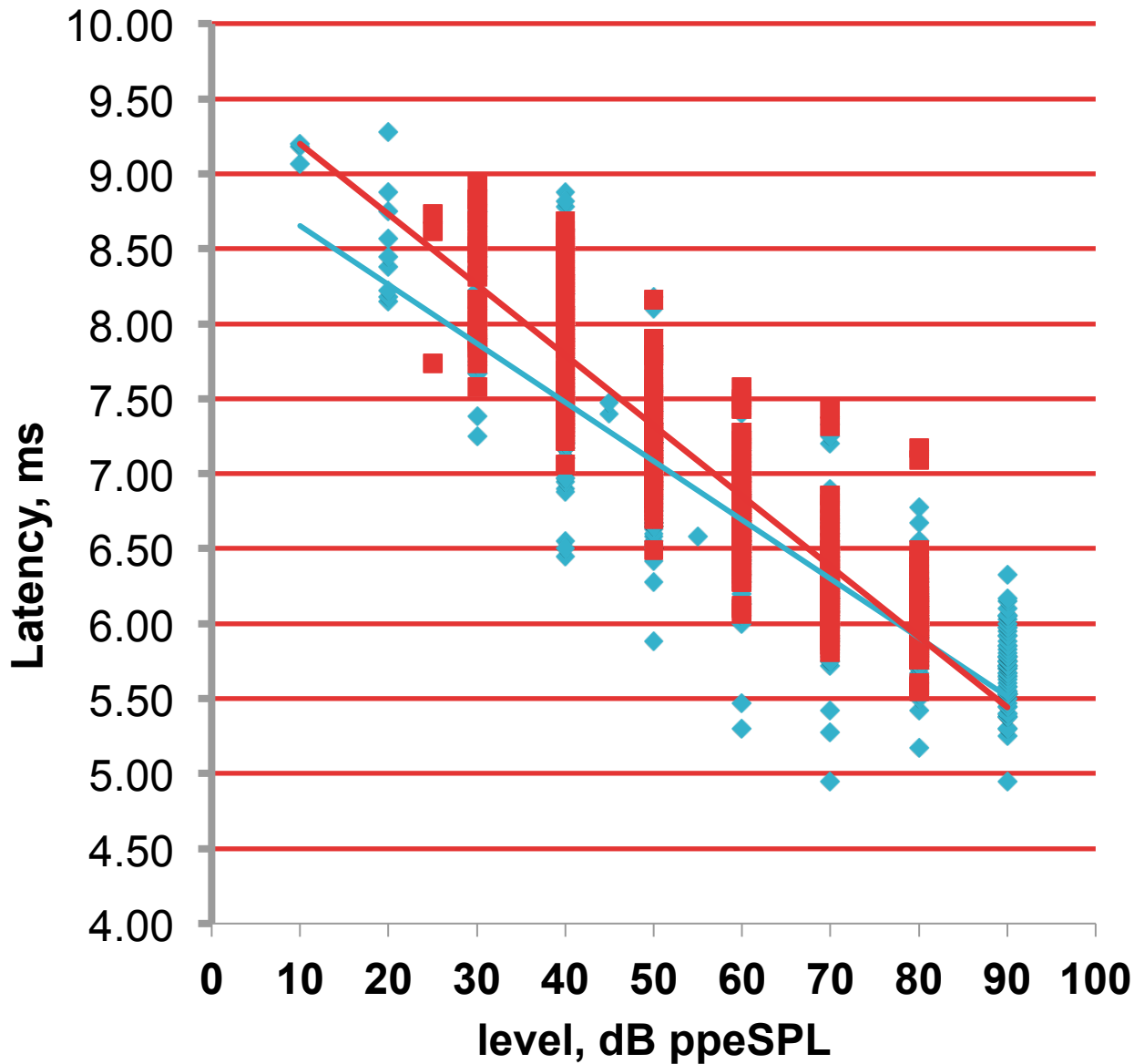


Reading Aloud: steady-state noise



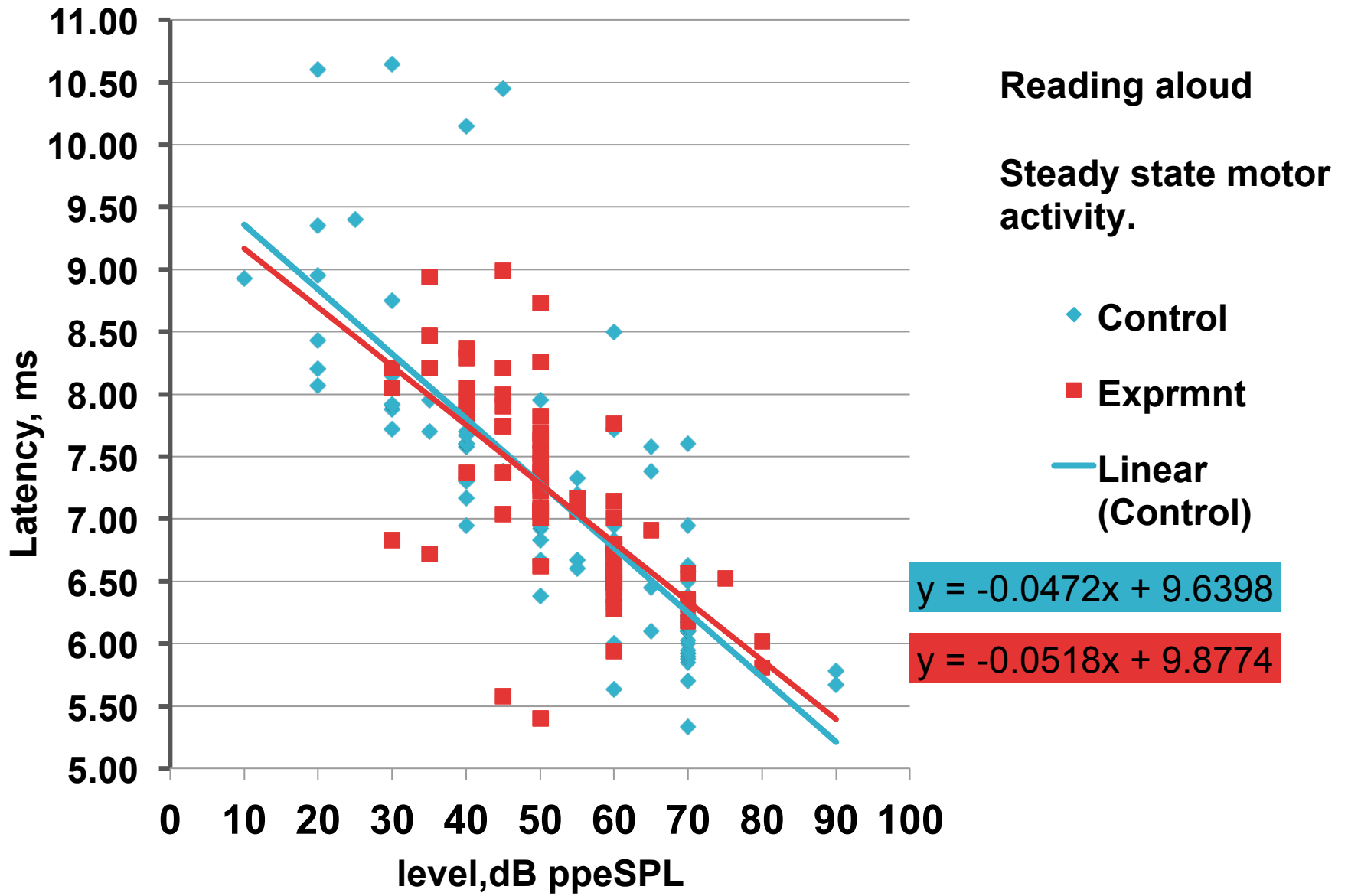
Intermittent Movement

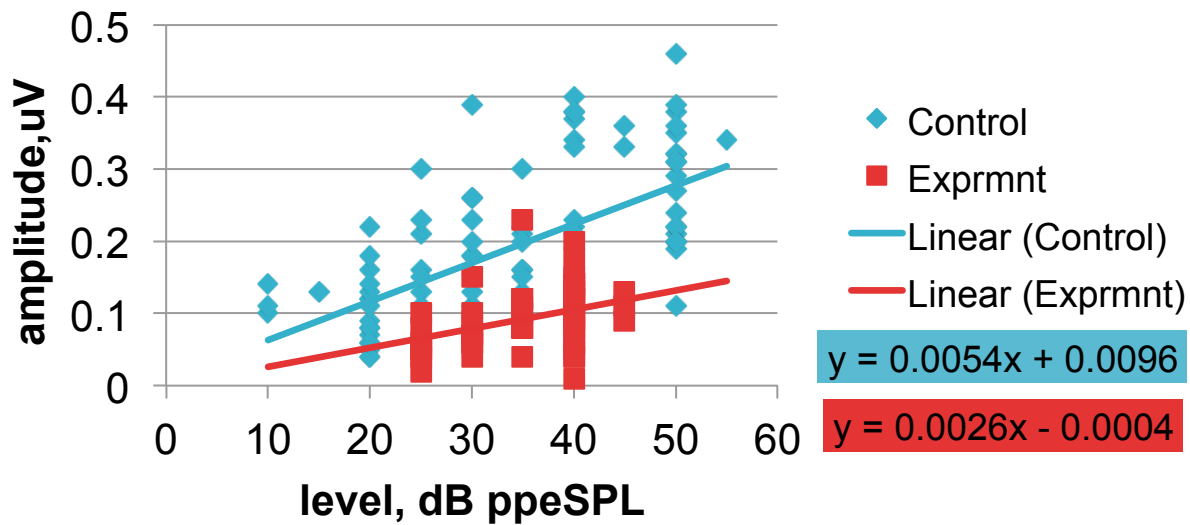
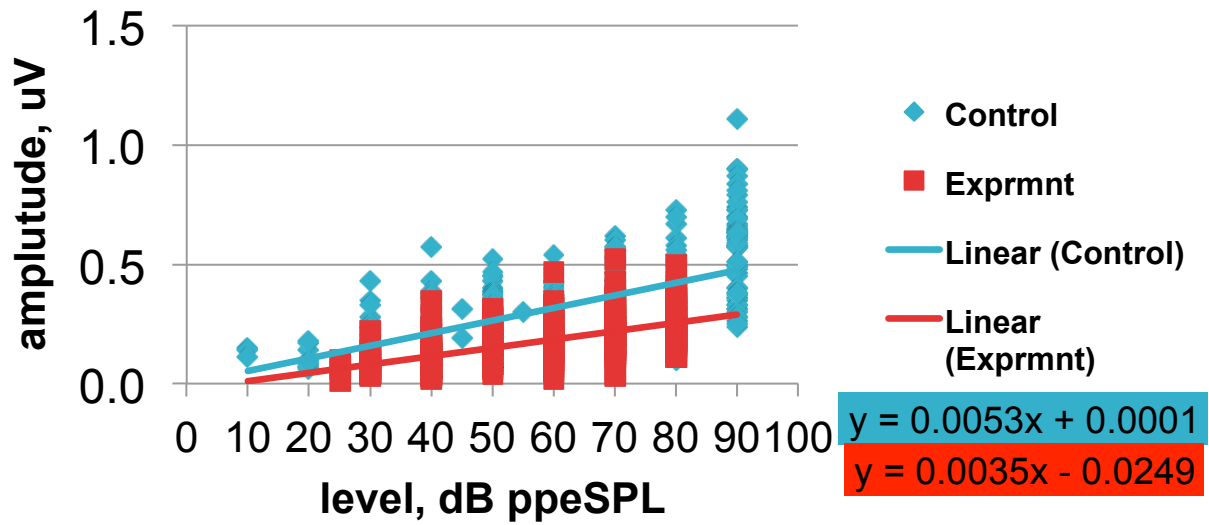




Quiet

- ◆ Control
- Exprmnt
- Linear (Control)
- Linear (Exprmnt)
- $y = -0.047x + 9.6692$
- $y = -0.0392x + 9.0453$





Summary of Experiment I



- In quiet, conventional signal processing and innovative signal processing are equivalent in terms of being able to obtain a wave V at low stimulus levels.
- In steady state induced motor noise, a 25-35% advantage for "experimental" methods is obtained at 50 and 60 dB ppe SPL (30 and 40 dB nHL).
- In intermittent induced motor noise, there is a 25% advantage for experimental methods at 50 dB dB ppeSPL.

Summary of Experiment I



- ABR wave V latencies are prolonged for "experimental" system compared to conventional.
-
- Amplitudes are smaller for ABRs obtained with the experimental system compared to a conventional system.

Discussion



- kalman-filter +*in situ* amplifier method (Vivosonic) had 25-35% better probability of ABR response present in motor noise conditions at near threshold levels.
 - ✦ Advanced signal processing methods are designed to extract response from noise.
 - ✦ Advantages may be increased for other band-pass settings
 - This is being tested in a controlled-lab setting.

Discussion



- Latencies prolonged for "experimental" method compared to conventional method.
 - Calibration?
 - Filtering can also induce some phase shifts
 - wave I – wave V IPLs were WNL
- Amplitudes smaller for "experimental" method
 - Amplitude of ABR is always contaminated by noise
 - Need to equate amplitudes on the basis of the noise floor.
 - Noise can inflate ABR wave V amplitudes

Experiment II: Clinical Verification



- **Purpose: move the system from the lab into the clinical setting**
- **Verify that the recordings made during infant wakefulness were comparable to those obtained in the lab setting with adults.**

Participants



- **Most infants referred to Tucson Medical Center for “natural sleep” ABR evaluation were under 6 months of age.**
 - Clinical verification study undertaken in 35 infants
- **Very few children, at our facility, are seen for ABRs between the ages of 6 months and 18 months of age.**
- **Older children are scheduled for ABRs under general anesthesia.**

ABR Evaluations using Vivosonic



- Treated as “typical” diagnostic ABR evaluations
- Compared to traditional equipment, using the Vivosonic involved the following:
 - Averaging began prior to baby falling asleep
 - Less “pausing” when child became somewhat active (e.g. sucking, slight motor activity).

Family and Baby Arrive



- **Consent signed**
- **Case history obtained**
- **Otoscopy**
- **OAEs and 1000 Hz tympanometry (if possible to help determine starting levels for ABR)**
- **Apply electrodes and insert earphones placed**

ABR Recording and Stimulus Parameters



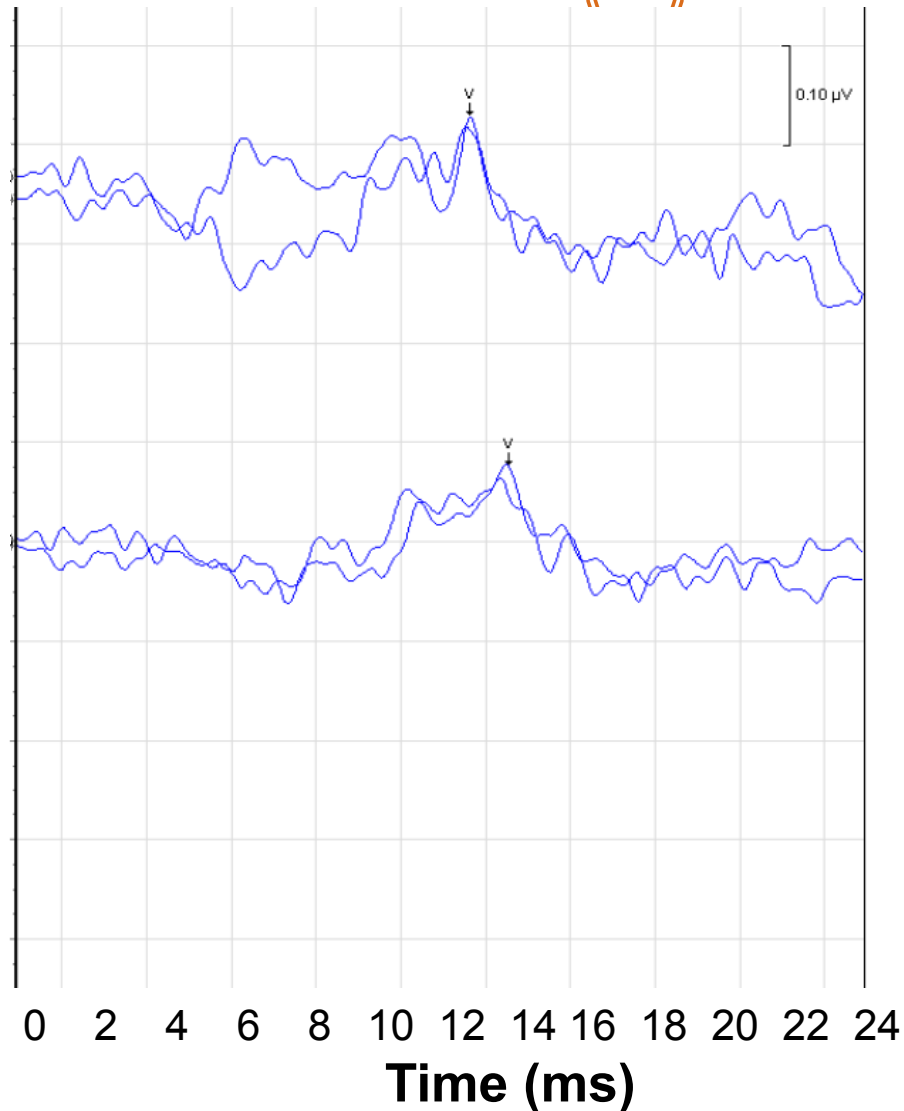
- Clicks
- Rate of 37.7/sec
- High pass filter of 30 Hz
- Low pass filter of 1500 Hz
- High frequency filter rolloff of 12 dB/octave
- Low frequency filter rolloff of 24 dB/octave
- Recording window: typically 20 ms

Stop criteria



- 1. How quiet is the ongoing EEG during the run?**
- 2. Visual inspection of the averaged waveform (does it look noisy)?**
- 3. Is there a wave V response (e.g. peak present and/or V trough deeper than other perturbations during recording)? Is the response in the latency range expected?**
- 4. If on 2nd run...is there replication?**

Examples ABRs recorded at 20 dBnHL



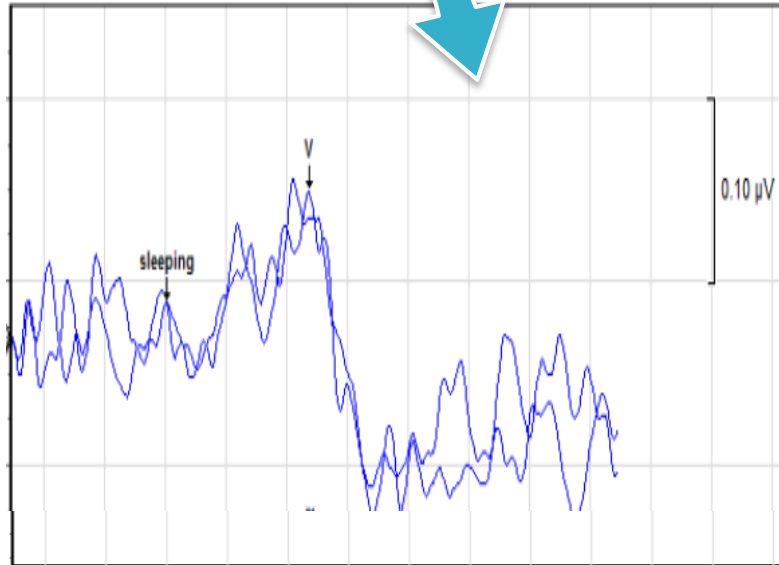
- Ongoing EEG was very quiet-no need to invoke Kalman Filter
- Clear peak and trough
- Replicated waveforms

Sleeping

vs.

Awake

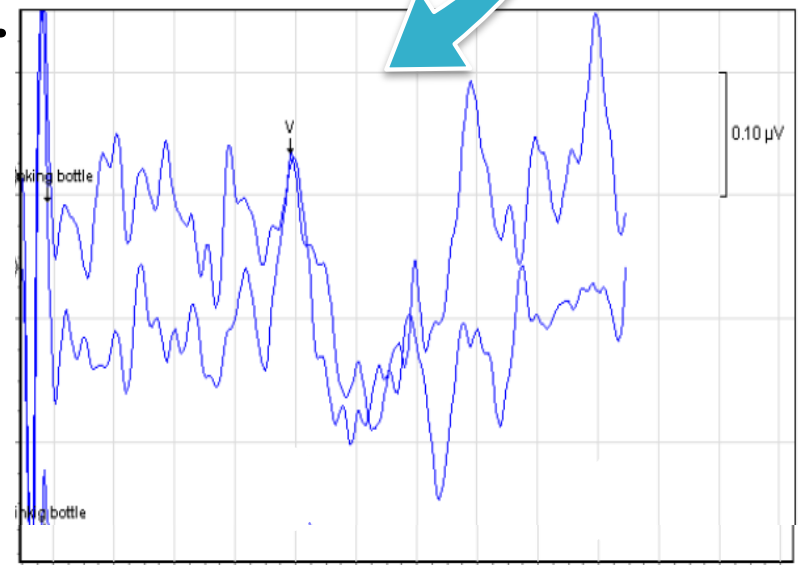
20
dBnHL



0 2 4 6 8 10 12 14 16 18 20
22 24

Time (ms)

**299 and 331
equivalent sweeps**

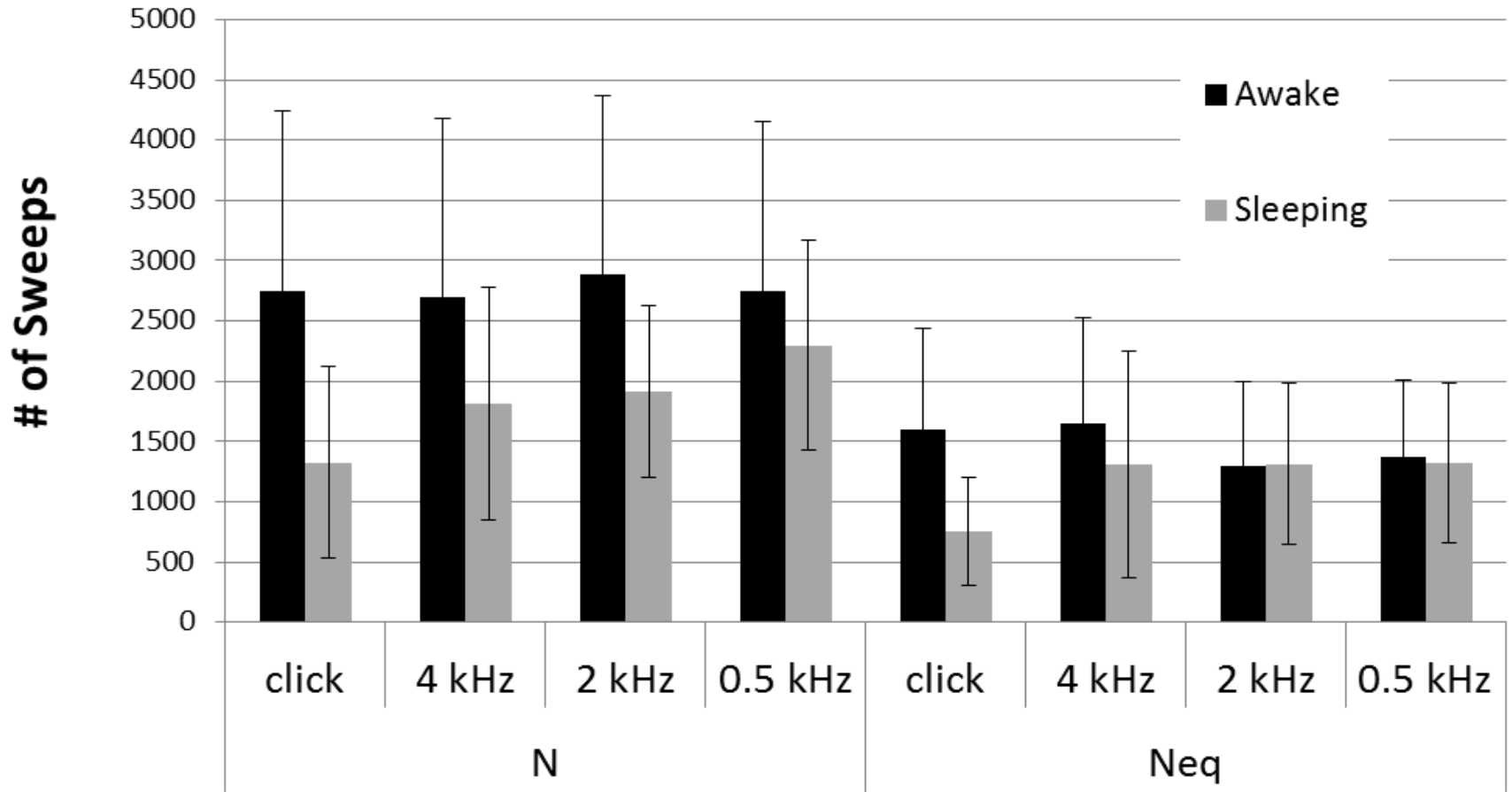


0 2 4 6 8 10 12 14 16 18 20
22 24

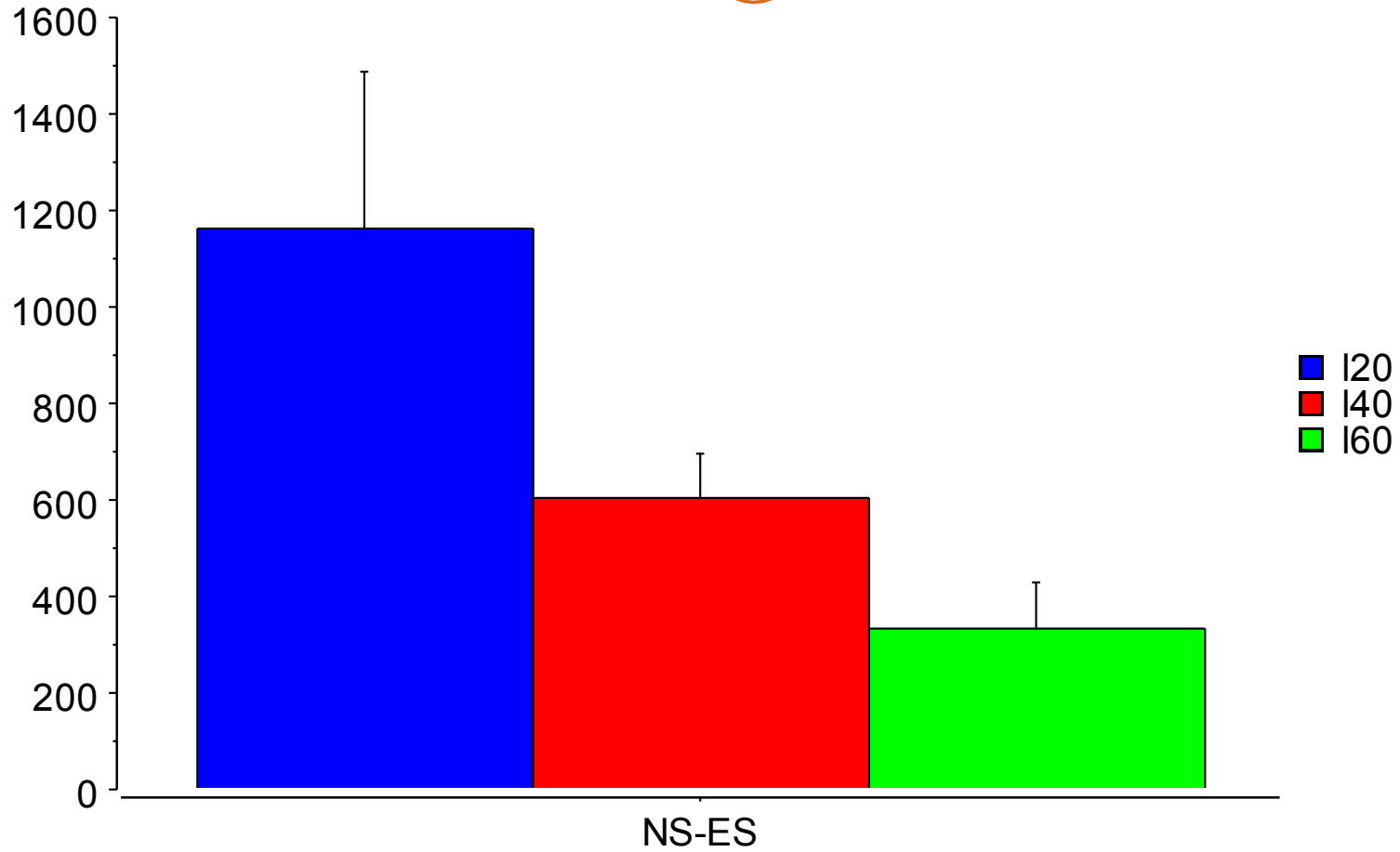
Time (ms)

**2257 and 1006
equivalent sweeps**

Effect of state on duration (# of sweeps) of trials



N Sweeps minus Equivalent Sweeps



Discussion



- Clinical verification indicated that the Vivosonic system could be used to obtain ABRs at near threshold levels in infants who were awake during testing.
- Clinician subjectivity regarding “acceptable noise level” during testing will affect results.
- On-line measures of response and noise levels are needed to provide clinicians the tools they need to make accurate estimates of thresholds from ABR tests.

Cost modeling example:

- For each noisy infant/child being evaluated the kalman-filtered EEG/ABR improves the chance of obtaining a response at near threshold levels by up to 35%.
- What does this mean in terms of costs?

What's it worth to you?



- 10 dB closer to true threshold?
 - Hearing aid fitting
 - Other diagnostic procedures
- 35% increased likelihood of obtaining a response?
 - Covert that to audiology time: estimate saving 10 minutes per patient
 - If cost of an eval is \$600/hour (all overheads considered) then that is \$100/patient.

A conservative example



- 3 natural sleep ABRs/day @ \$600.00/test
- Advanced signal processing (kalman+*in-situ* amplifier) results in a 35% increased likelihood of being able to obtain a near threshold response during steady or intermittent noise.
- This could translate to 10 minutes of time saving/test.
- \$300.00 savings/day.

The Jackpot



- For every patient that can be tested without sedation/anesthesia, the cost savings is up to \$5,000.00/test.
- Given your case-load, how many patients/month would be eligible for natural sleep (or moderately quiet wakefulness) ABRs?

Other scenarios



- Ability to obtain an ABR at 20-30 dB nHL in a moderately wakeful may result in cost savings if combined with:
 - Tympanometry results
 - OAE results
- If a “pass” for these quasi-screening results, then it may be more appropriate to follow the infant using behavioral methods.

Features of the system we did not test



- Wireless connection (blue-tooth)
- 1 vs. 2 channels

How much cost-savings from use of wireless connection of amplifier to computer?



- We did not test this feature in our lab or clinic-based verification studies.
- The comparison data are obvious
 - 100% performance for wireless system
 - 0% performance for conventional hard-wired system.
- How many times did you wish you could test an infant while driving them around in a car to induce sleep??
 - N= 1 (me)
 - About 1,000,000

Other features

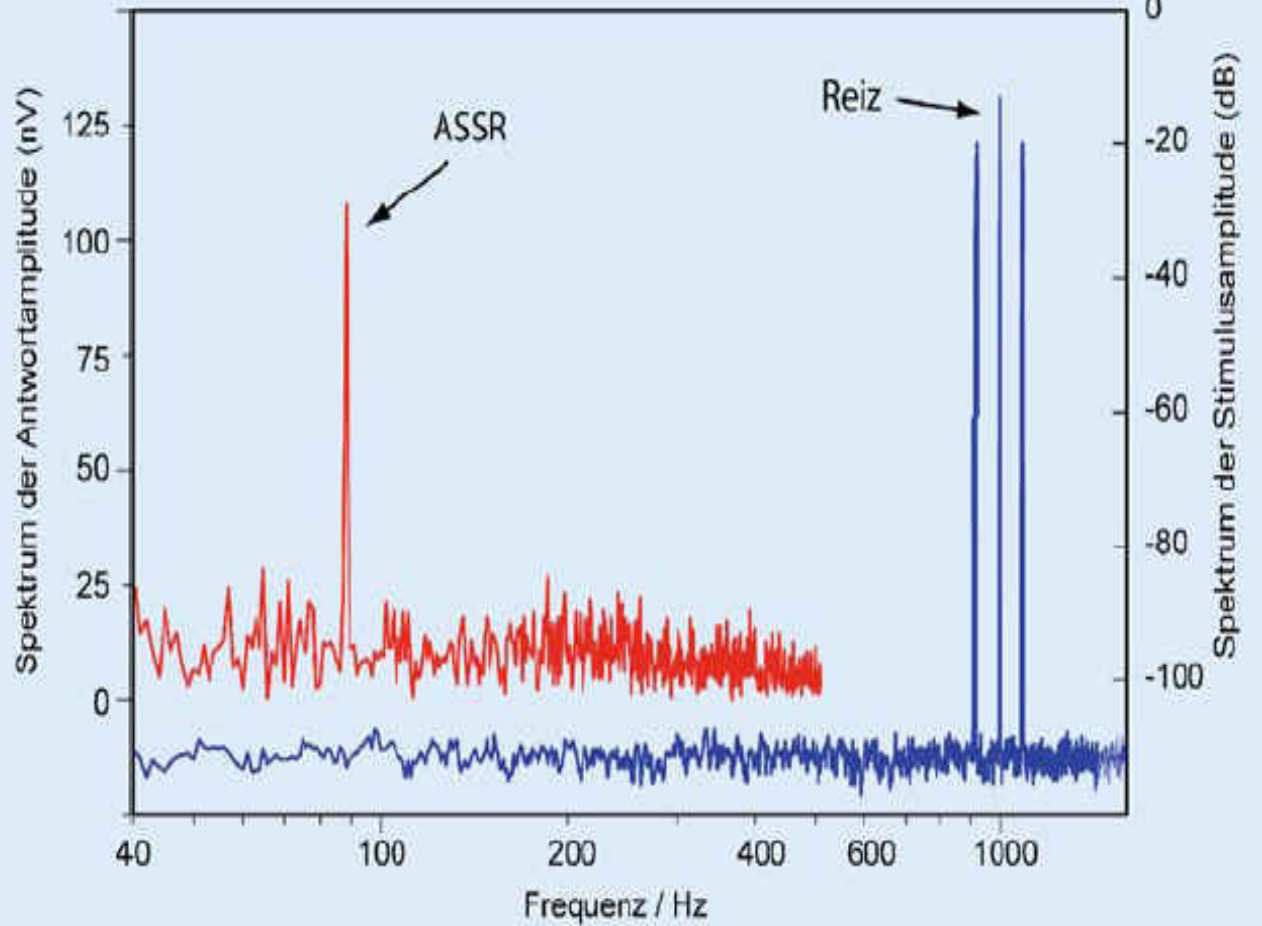
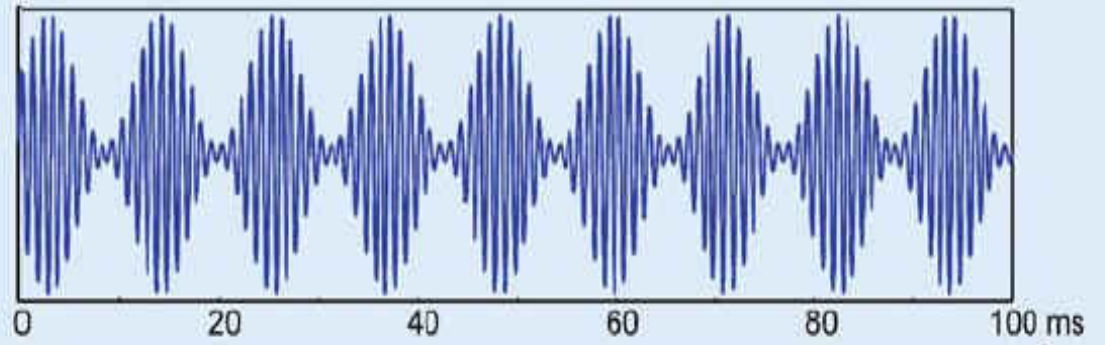


- Currently, the wireless system is limited to 1-channel.
- Does the benefit of wireless out-weigh the cost of having only 1 channel ?
 - How often do you use information from the second channel?
 - Put a \$\$ value on that and compare it to your estimated value of the wireless connection.
- Positive or negative net effect?

Cost-Modeling Summary



- Costs and benefits must be considered on a “practice-pattern” basis.
- Costs and benefits can be modeled using strict or lax criteria.
 - Strict criteria = conservative estimate of savings
 - Lax criteria = greater estimate of savings
- Empirical data suggests up to a 35% “advantage” for kalman-filtered + in-situ amplifier (2 features of Vivosonic) ABR.
- Other features (e.g. wireless) may result in additional benefits/cost-savings but should be calculated with respect to limitations (e.g., 1-channel).



Auditory Steady State Responses in Awake Infants



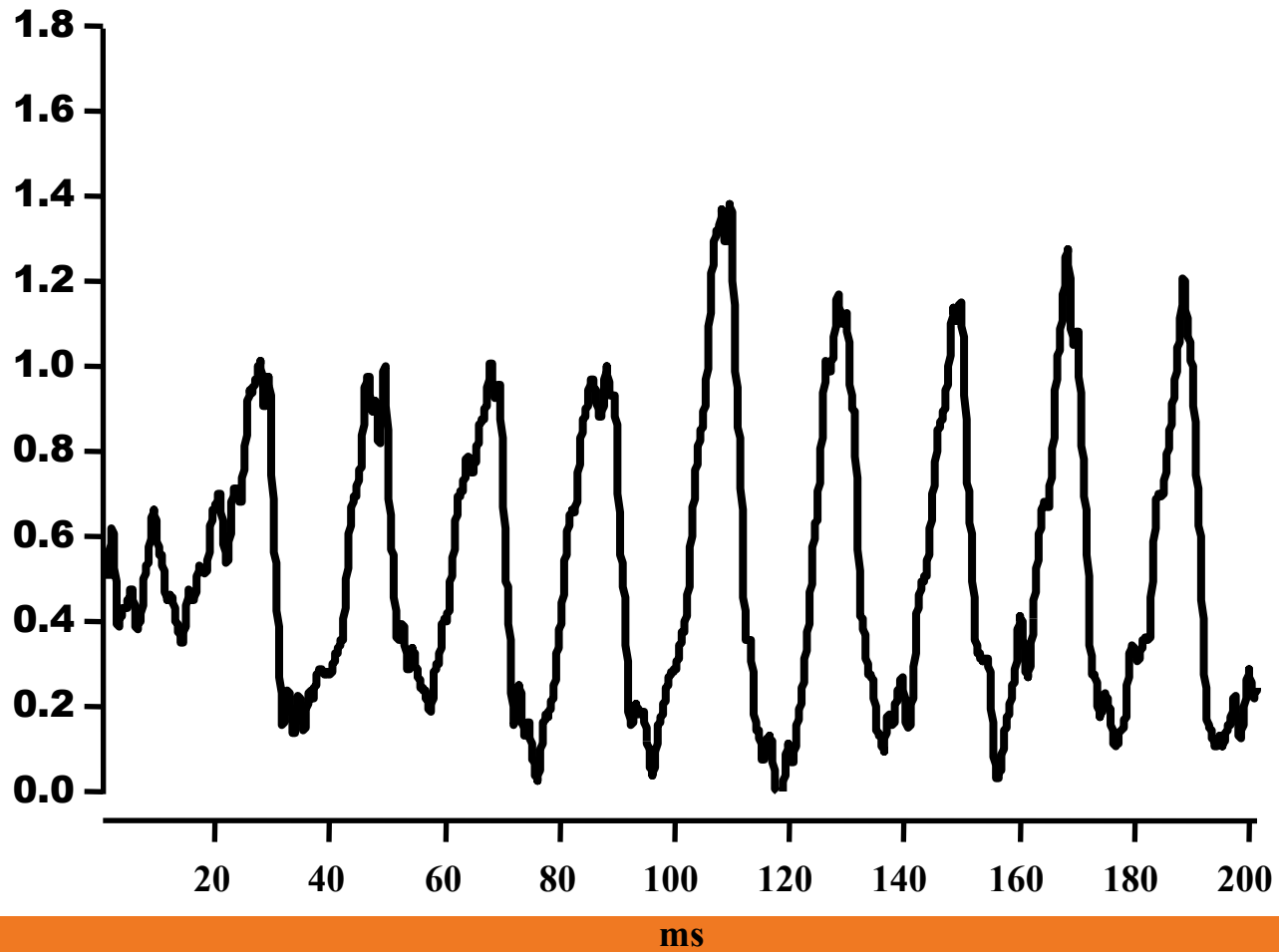
**BARBARA CONE, PH.D.
UNIVERSITY OF ARIZONA
TUCSON, ARIZONA**

Introduction



- ASSRs have their place in the tool-box for “evoked response audiometry”
- Threshold estimation
- Auditory (temporal) processing
- Speech perception deficits

2000 Hz CF, 50 Hz MF

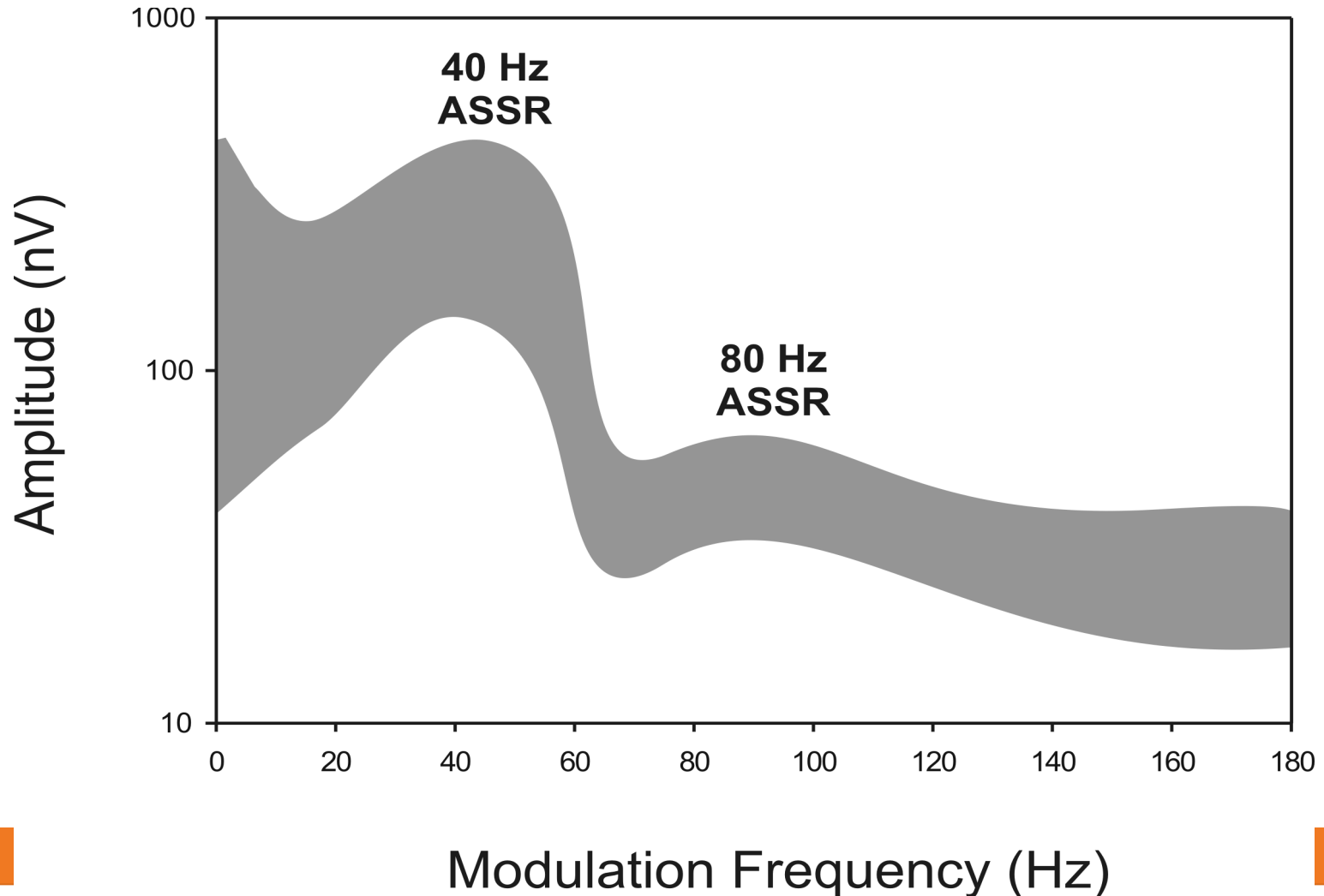


ASSR Characteristics



- Present at near threshold levels.
- Present for a wide range of modulation frequencies, from less than 10 Hz to over 150 Hz.
- Responses for rates ≥ 80 Hz have many response characteristics similar to ABR.

ASSR Amplitude as a function of modulation frequency



ASSR in Infants

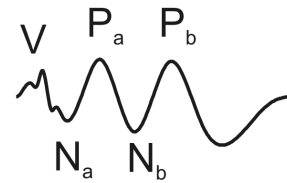
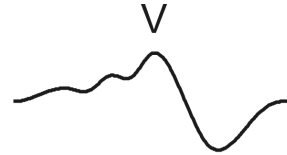


- Response properties in sleeping infants are similar to those observed for ABR when high (>80 Hz) modulation rates are used.
- Responses in sleeping infants for lower modulation rates (<50 Hz) are inconsistent or absent.
- There is a strong influence of neurodevelopment and sleep stage on ASSRs for lower modulation rates.
 - This is also seen for transient responses: MLR and CAEP

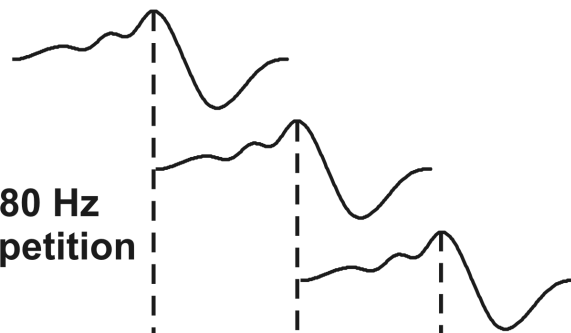
ASSRs: 80 Hz and 40 Hz



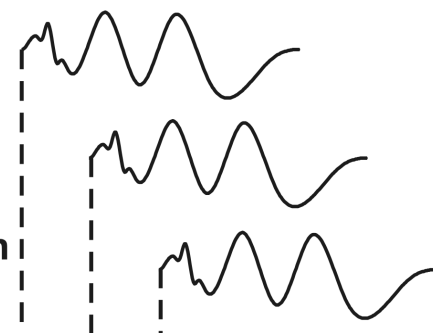
transient



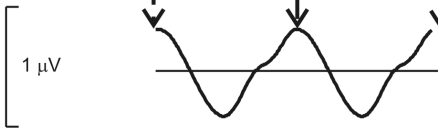
80 Hz repetition



40 Hz repetition

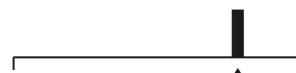


steady-state



20 ms

100 ms

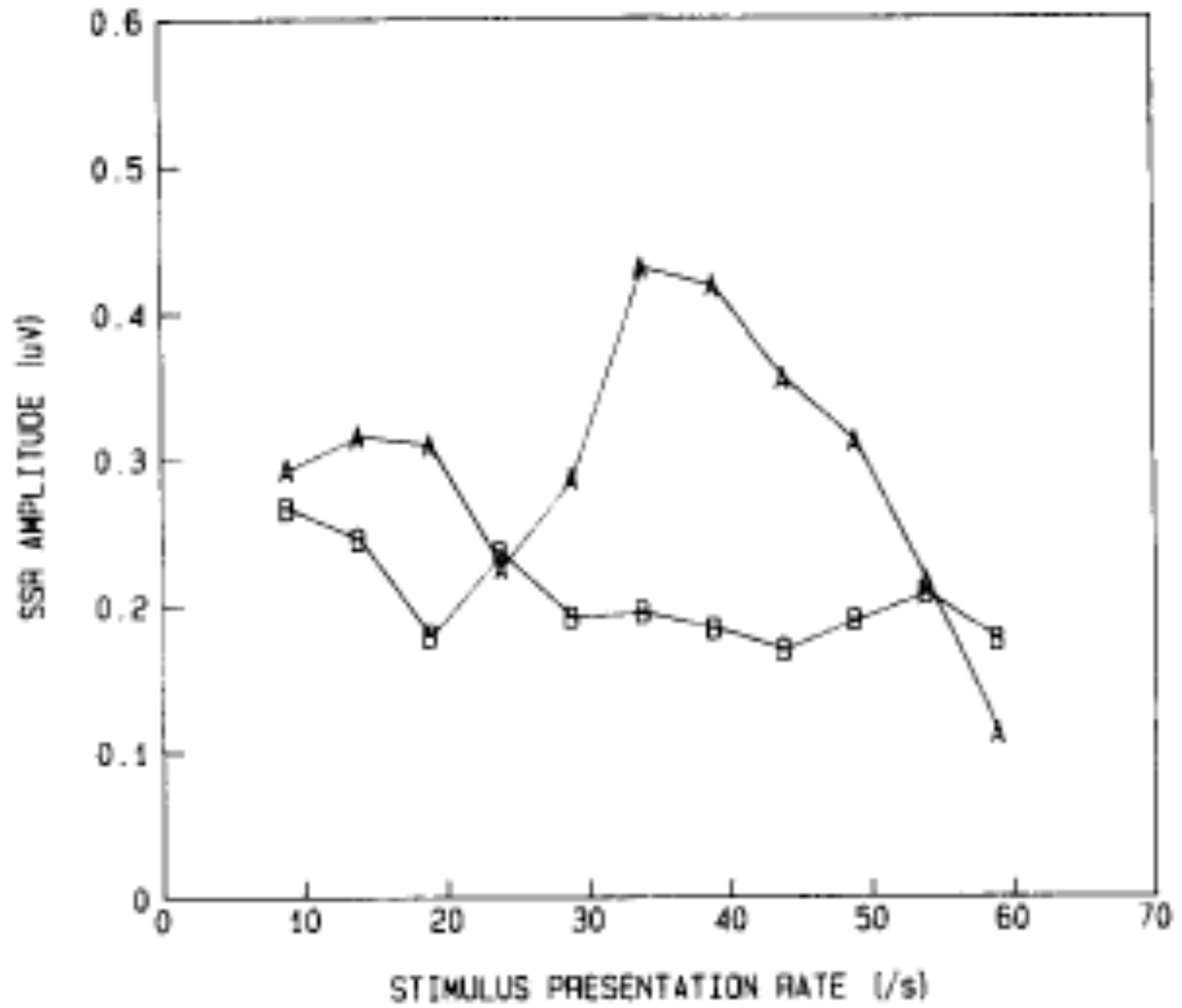


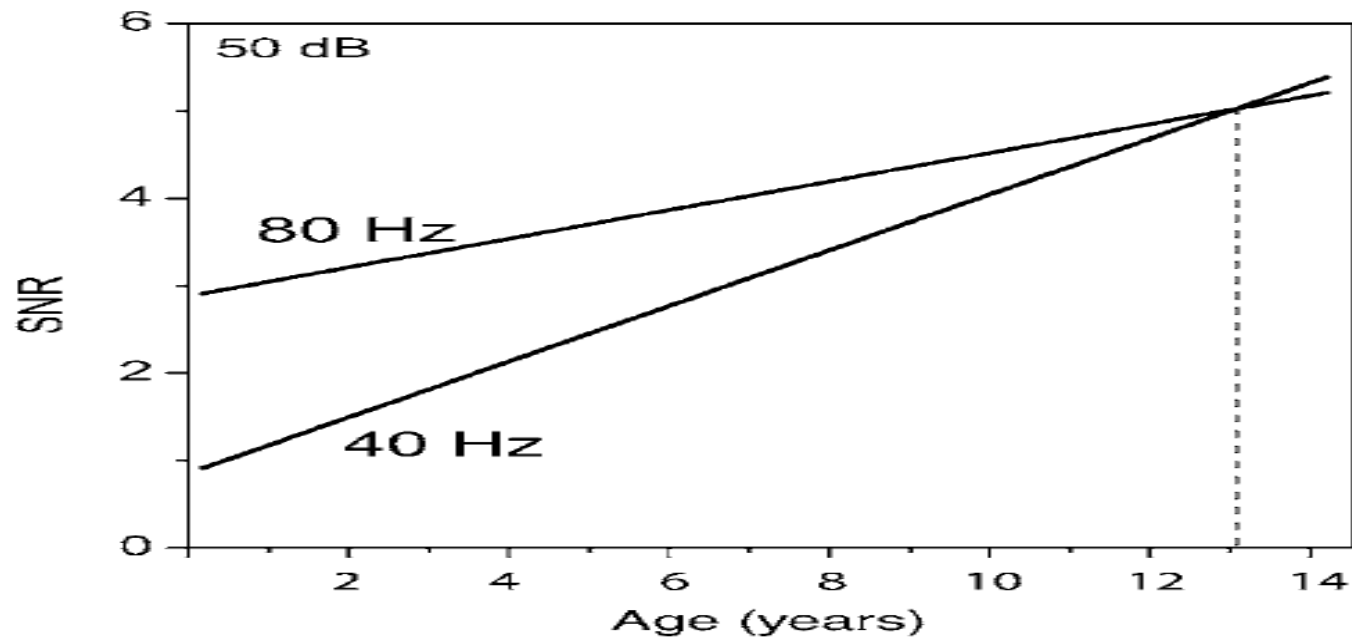
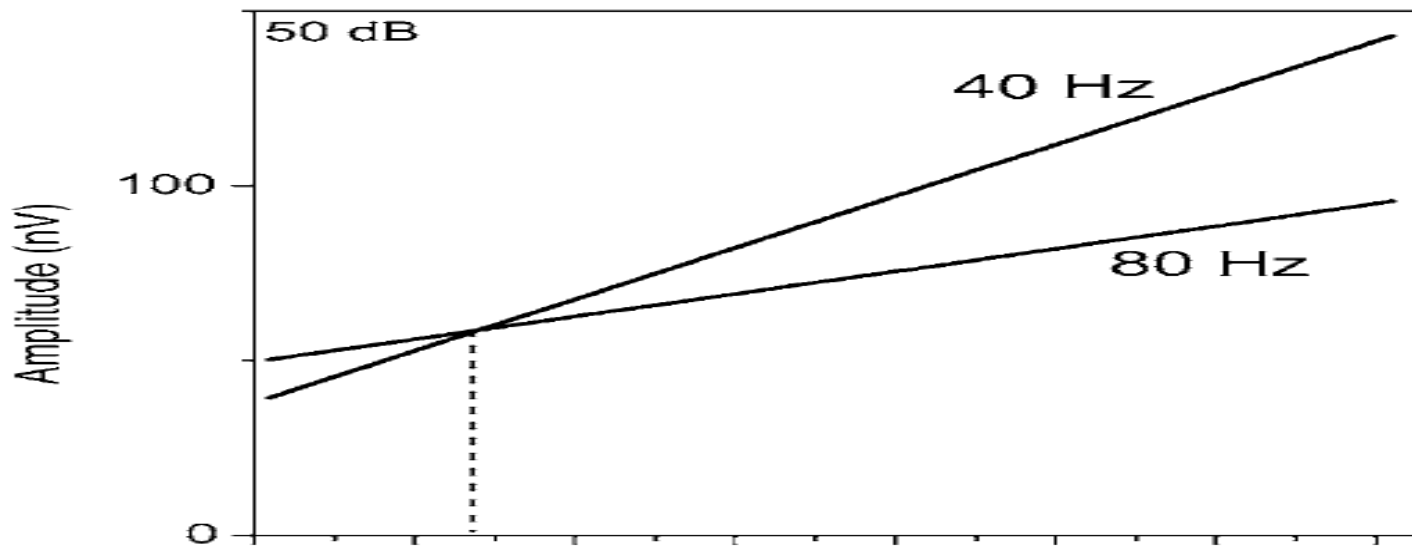
80 Hz



40 Hz

Stapells, 1988





40 Hz ASSR



- The 40 Hz ASSR is generated at the level of the auditory cortex.
- It has a larger amplitude than 80 Hz ASSR (generated at the brainstem).
- 40 Hz ASSR can be obtained in quiet wakefulness in older children or adults.

Gap in Knowledge



- Very sparse data exist for development of the “40 Hz ASSR” (and its transient counterpart, the MLR) in human infants.
- Our aims were to address this gap by obtaining ASSRs at low (20 and 40 Hz) modulation rates in infants < 1 year tested while awake.

40 Hz ASSR in infants



- Are 40 Hz ASSR present in infants tested while awake?
- Are ASSRs present in infants at lower modulation rates?
- How do these differ from those found in adults?
- We hypothesized that ASSRs at 40 Hz would be present based upon previous results with transient-evoked cortical responses.
 - We also hypothesized that they would be of relative lower amplitude/power than in adults owing to immaturity of cortical mechanisms for rate-following and temporal processing.

Methods



- Participants:
- 12 infants, age range 4-11 months
- 9 adults, age range 20-26 years
- All passed TEOAE and/or pure tone threshold screening tests.
- All subjects tested while awake and quietly alert.

Stimuli



- Quasi-steady state 1 kHz tone burst trains presented at 70 or 80 dB peSPL.
- Rates were 20, 40 and 80 Hz.
- Order of modulation rate presentation was randomized across subjects.
- Monaural presentation to right ear using EAR 3A insert phones.

Stimuli for ASSRs



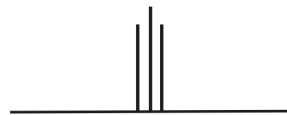
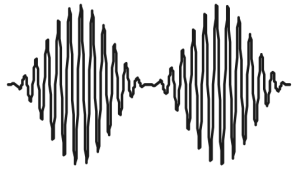
Time

Frequency

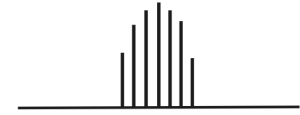
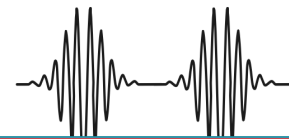
Time

Frequency

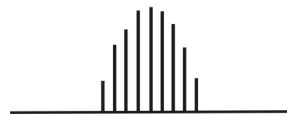
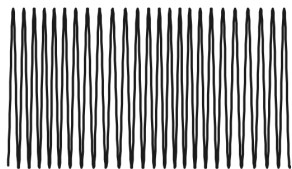
AM



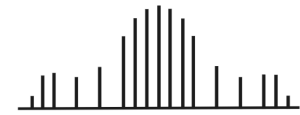
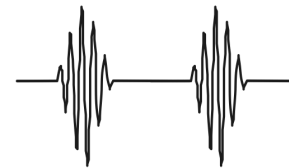
\sin^3



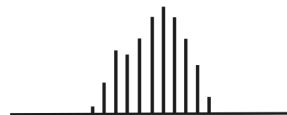
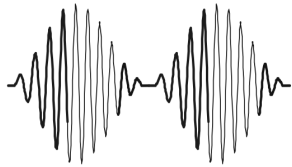
FM



tone



MM



noise



25 ms

0

2000 Hz

25 ms

0

2000 Hz

Response Acquisition

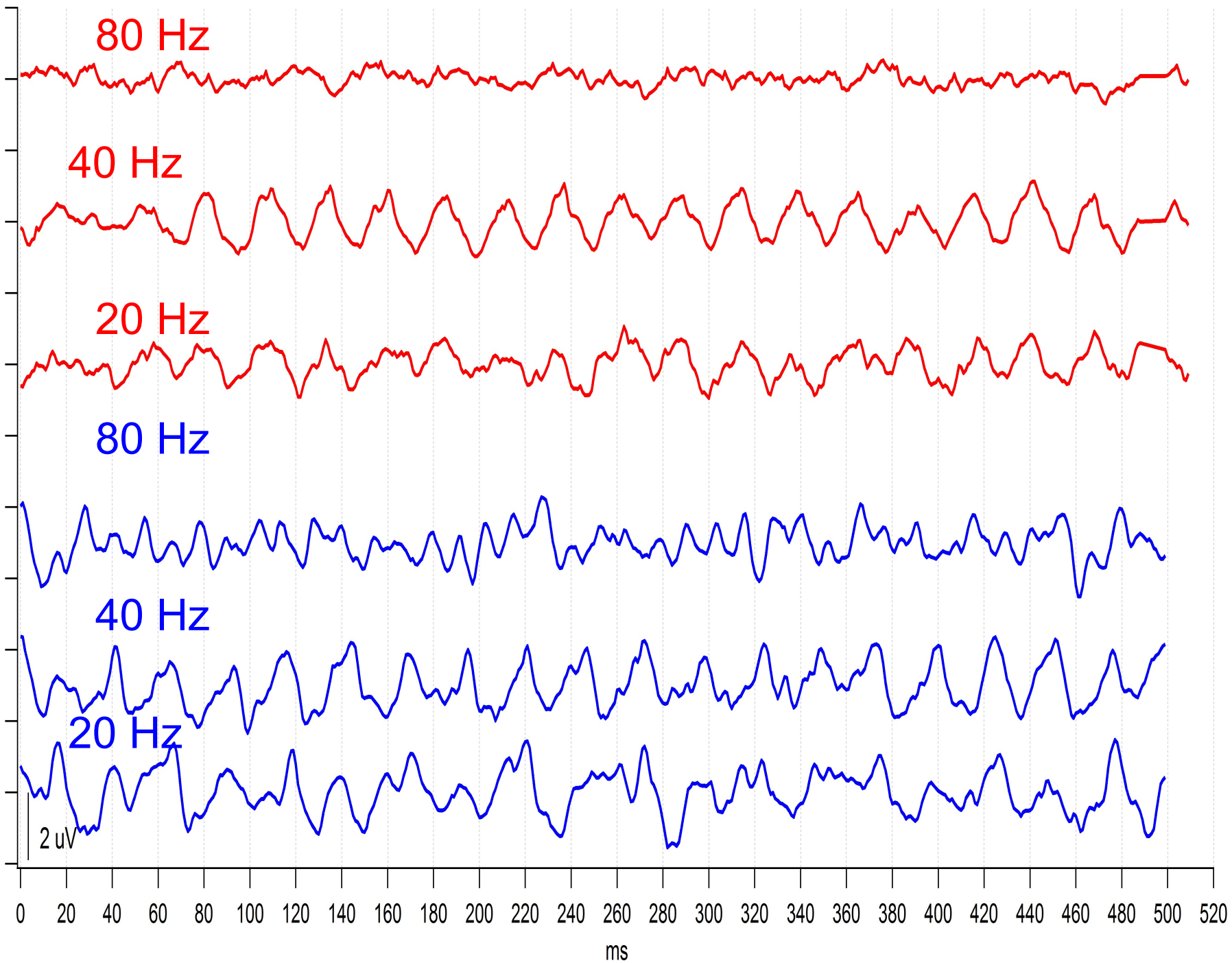


- Responses obtained using Intelligent Hearing Systems Smart-EP system.
- Epoch: 500 ms
- Filtering: 10-100 Hz @ 40 and 80 Hz, 1-100 for adults at 20 Hz.
- Amplification: 100K
- 512-1000 artifact free samples obtained for each rate.

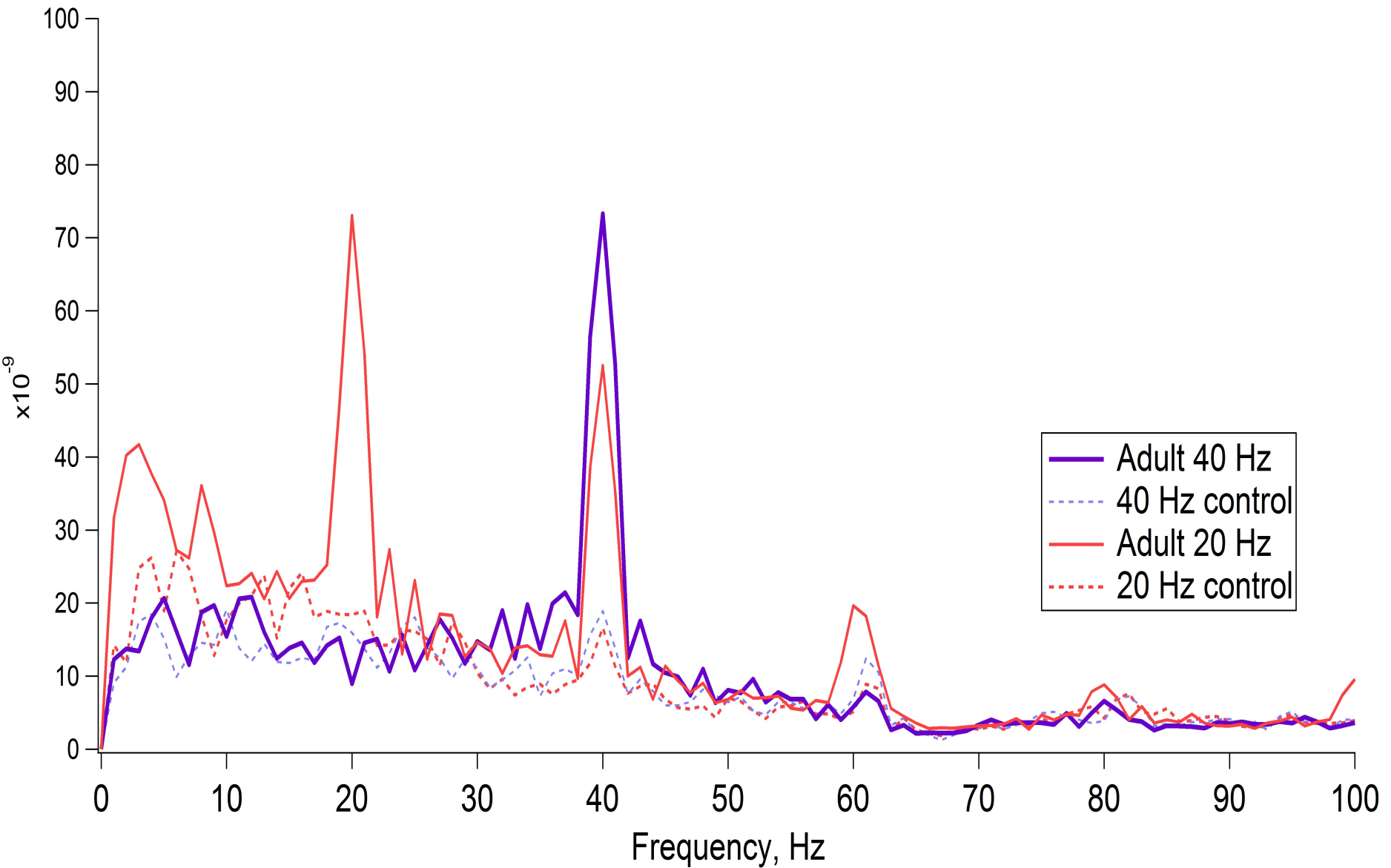
Data Analysis



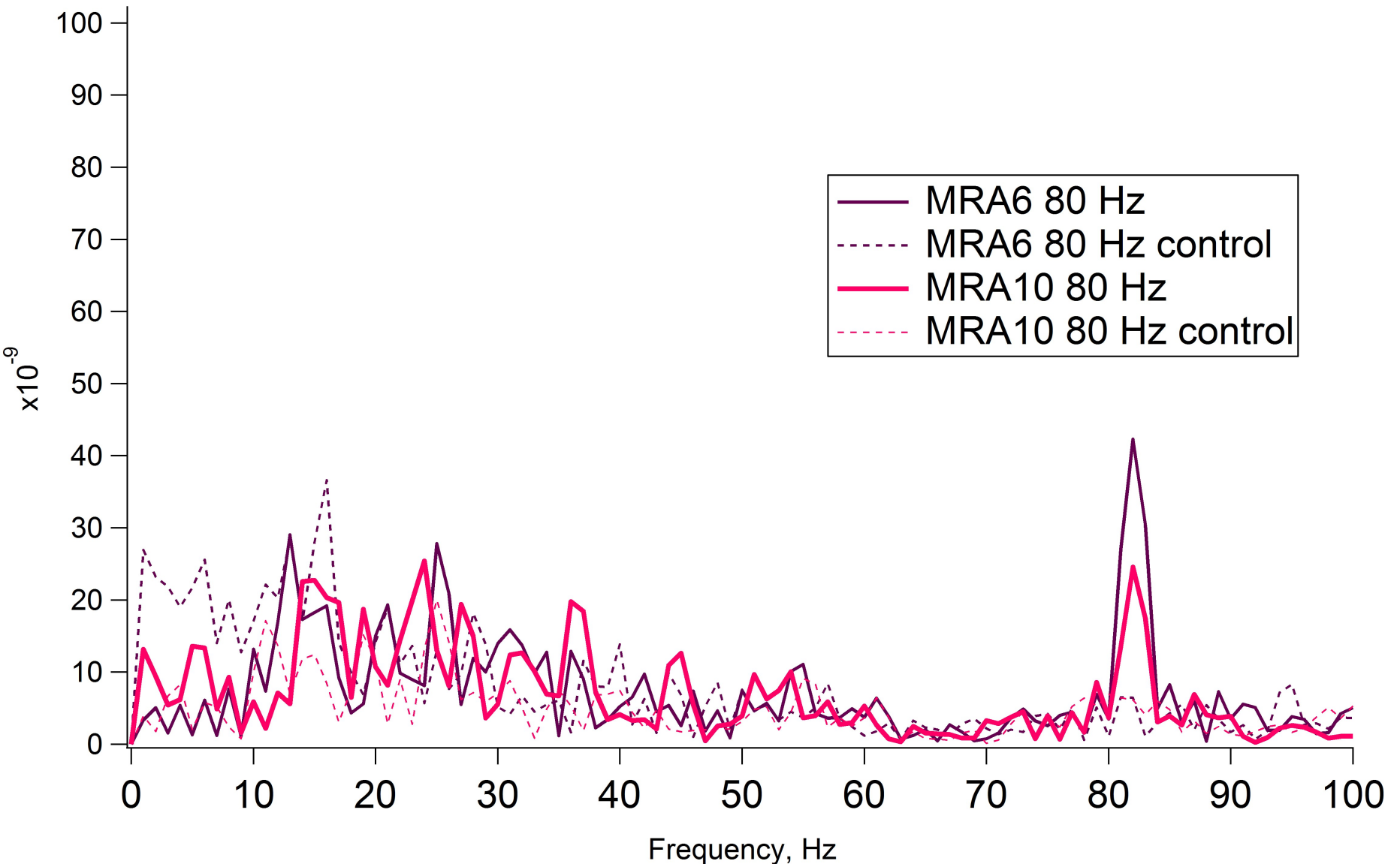
- Power spectra derived for each response.
- Peak-to-peak amplitude determined for each response.
- Grand mean average spectra and amplitudes as a function of rate were calculated.



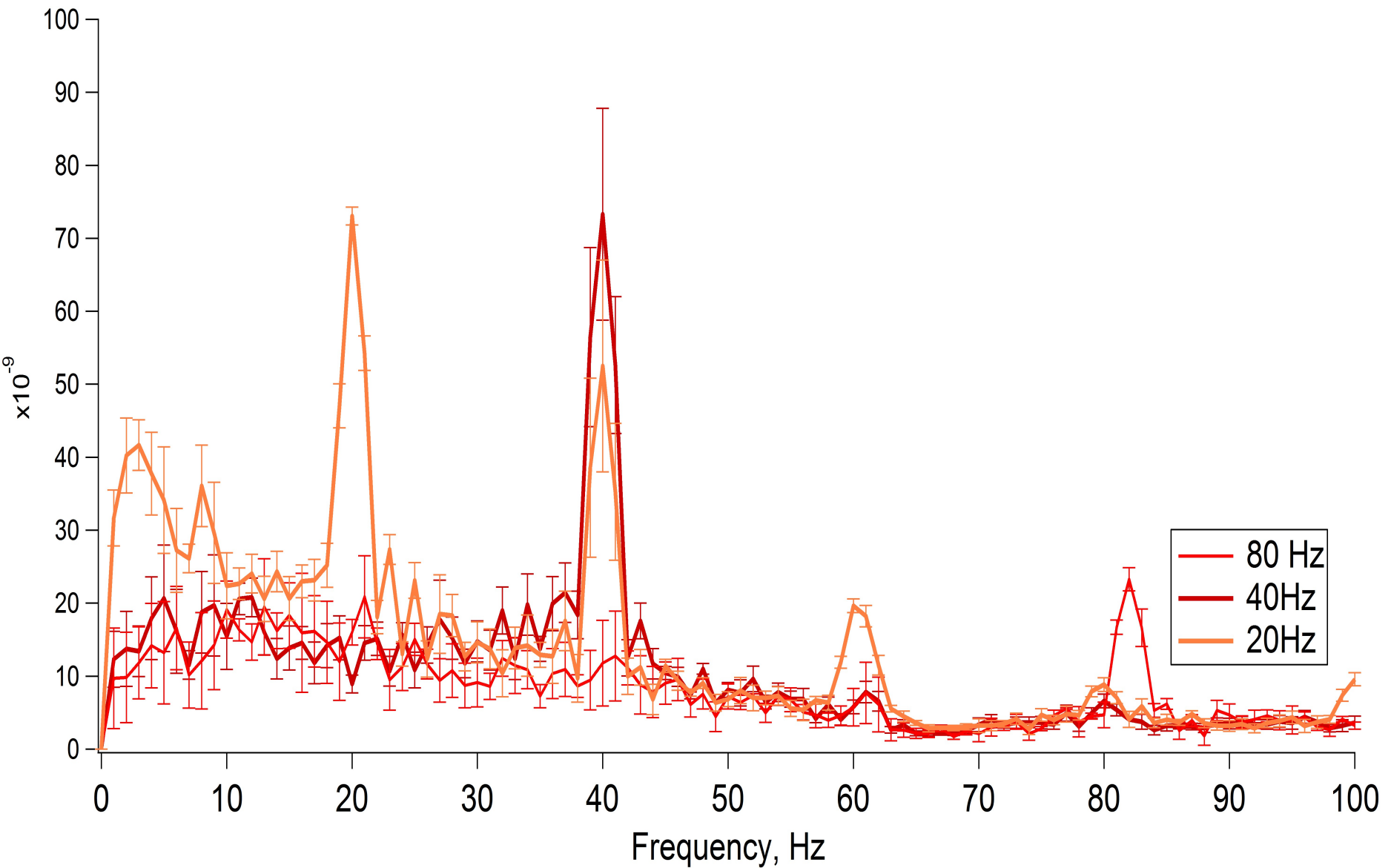
Control vs test recordings, Adults



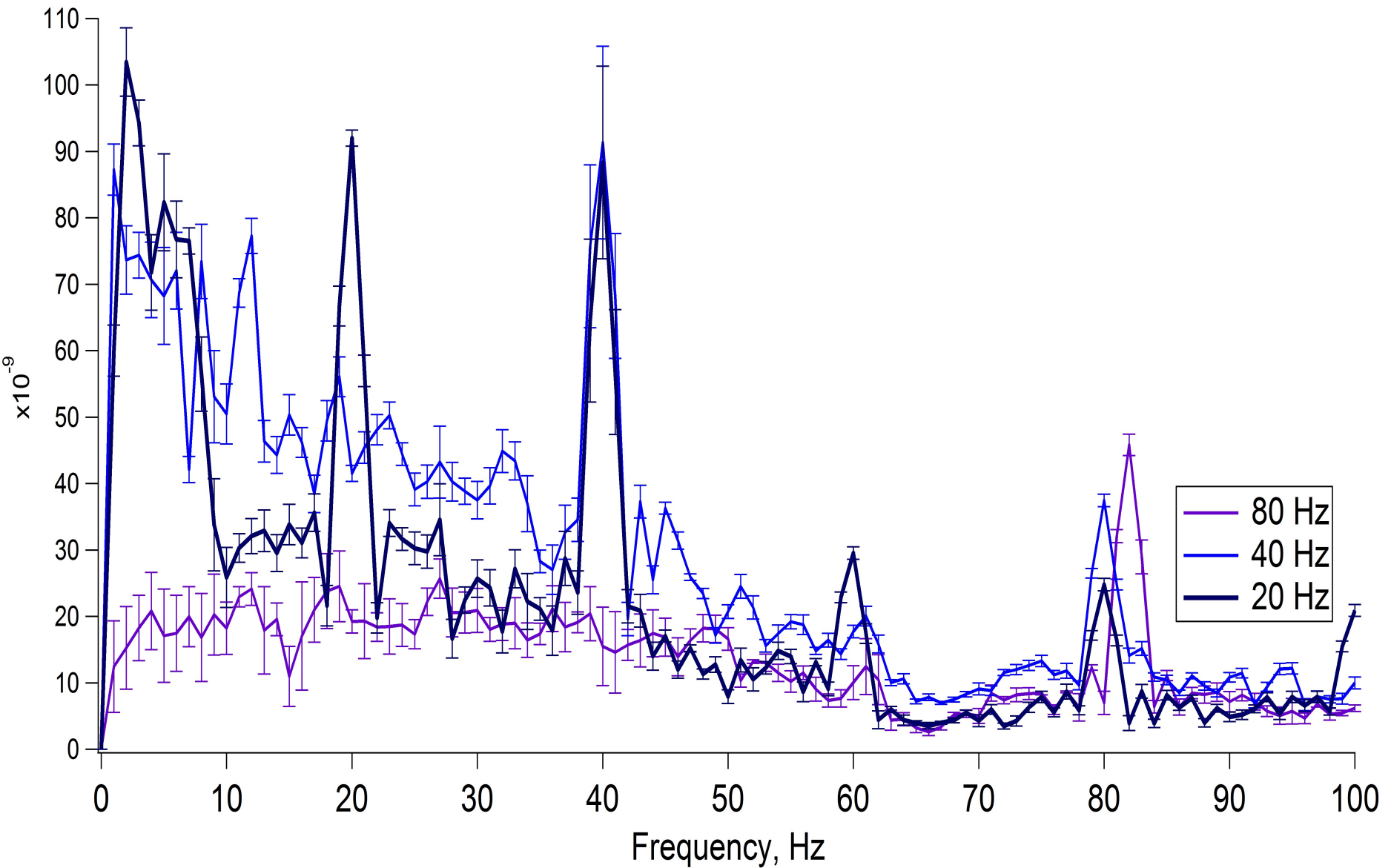
Control vs test recordings, Adults



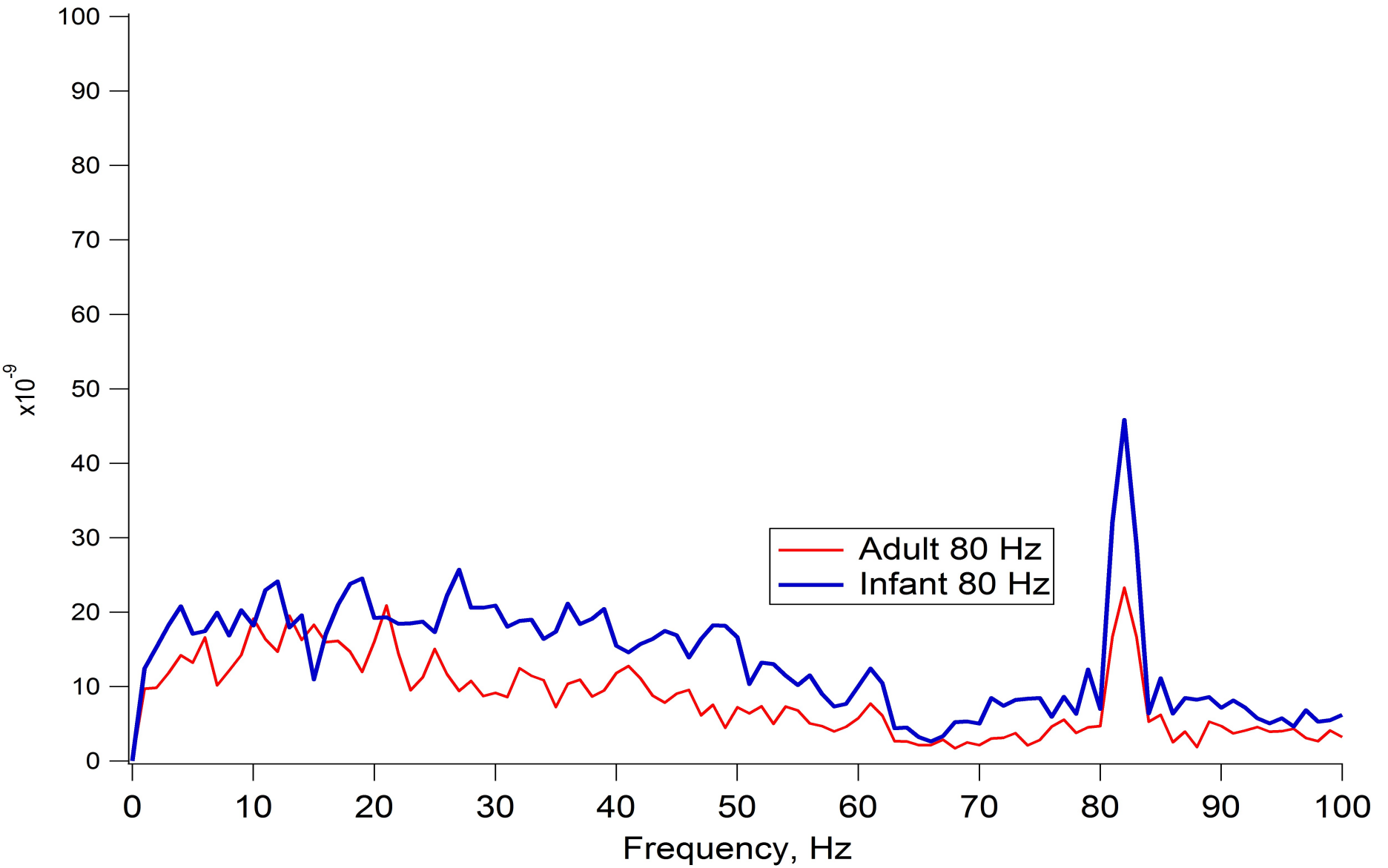
Grand mean spectra for adults



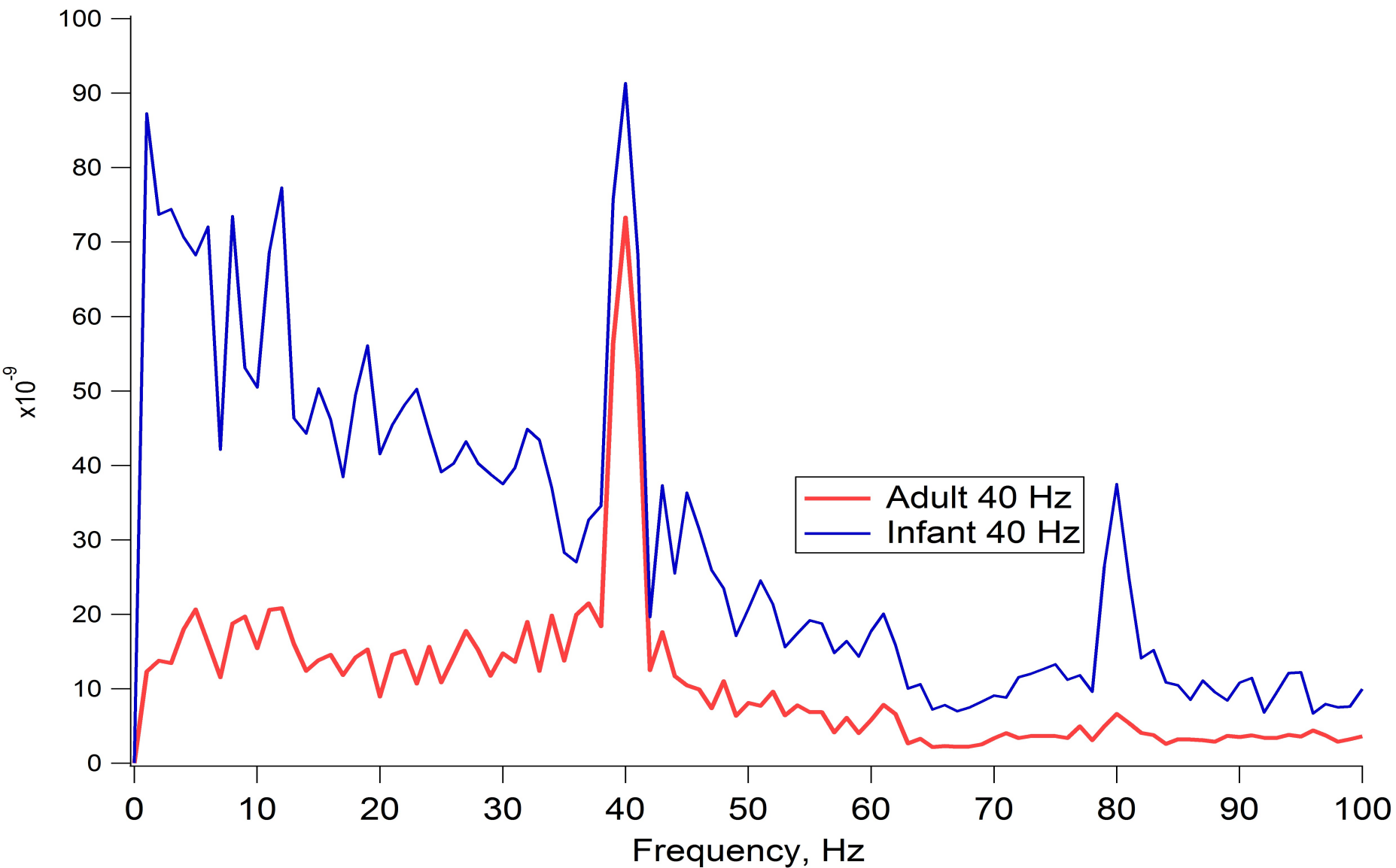
Grand mean spectra, infants



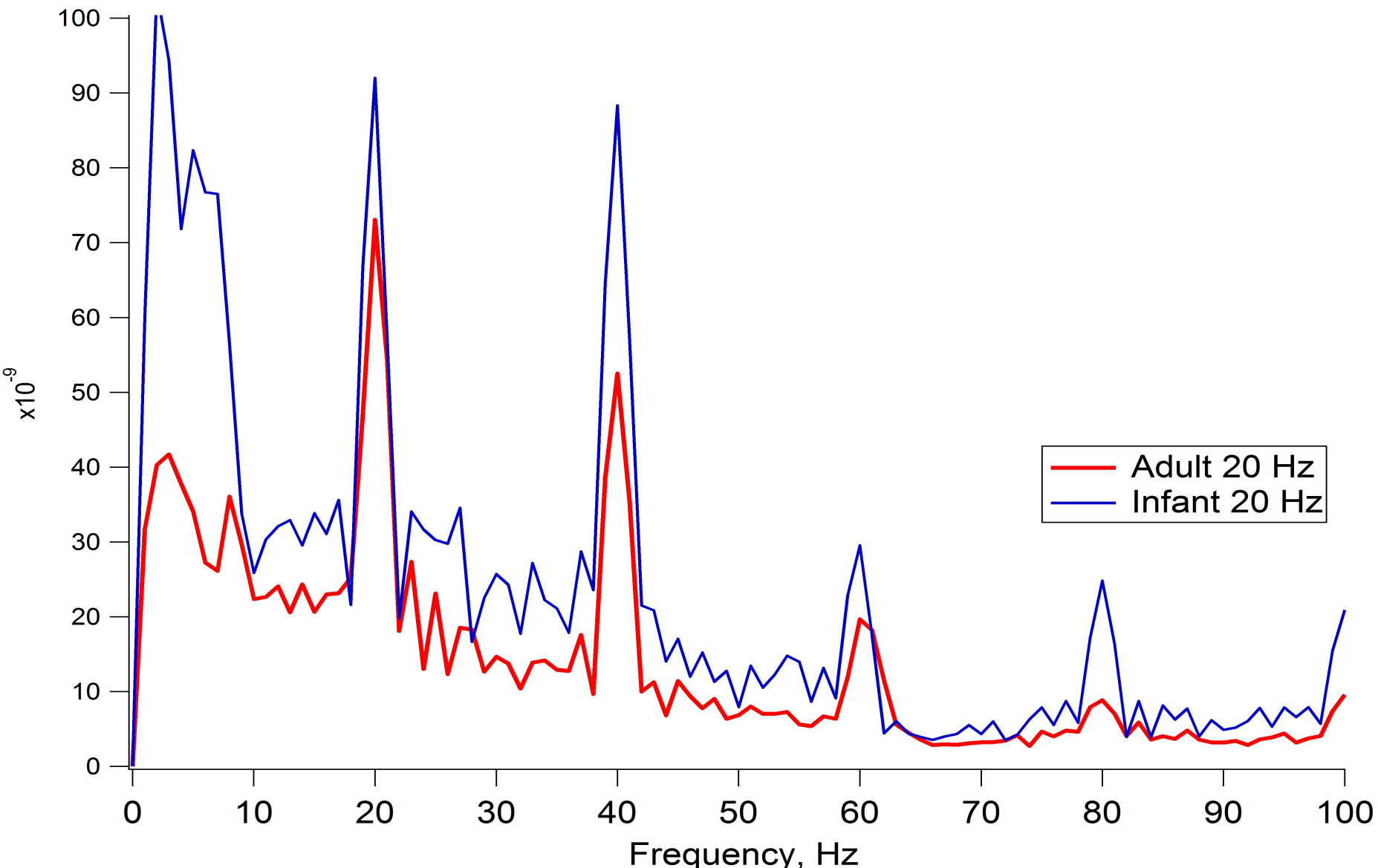
Adult vs. infant at 80 Hz



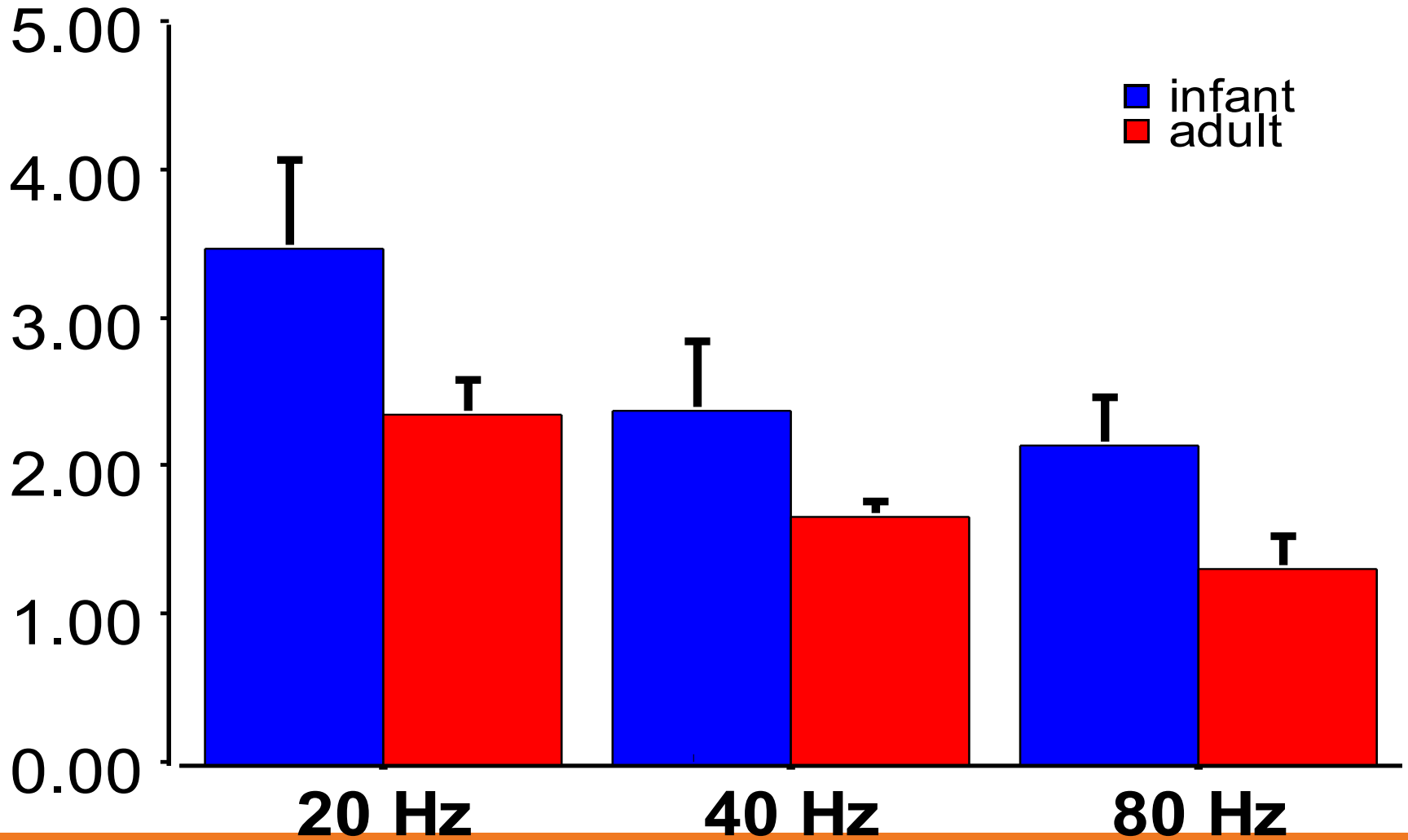
Adults vs Infants 40 Hz



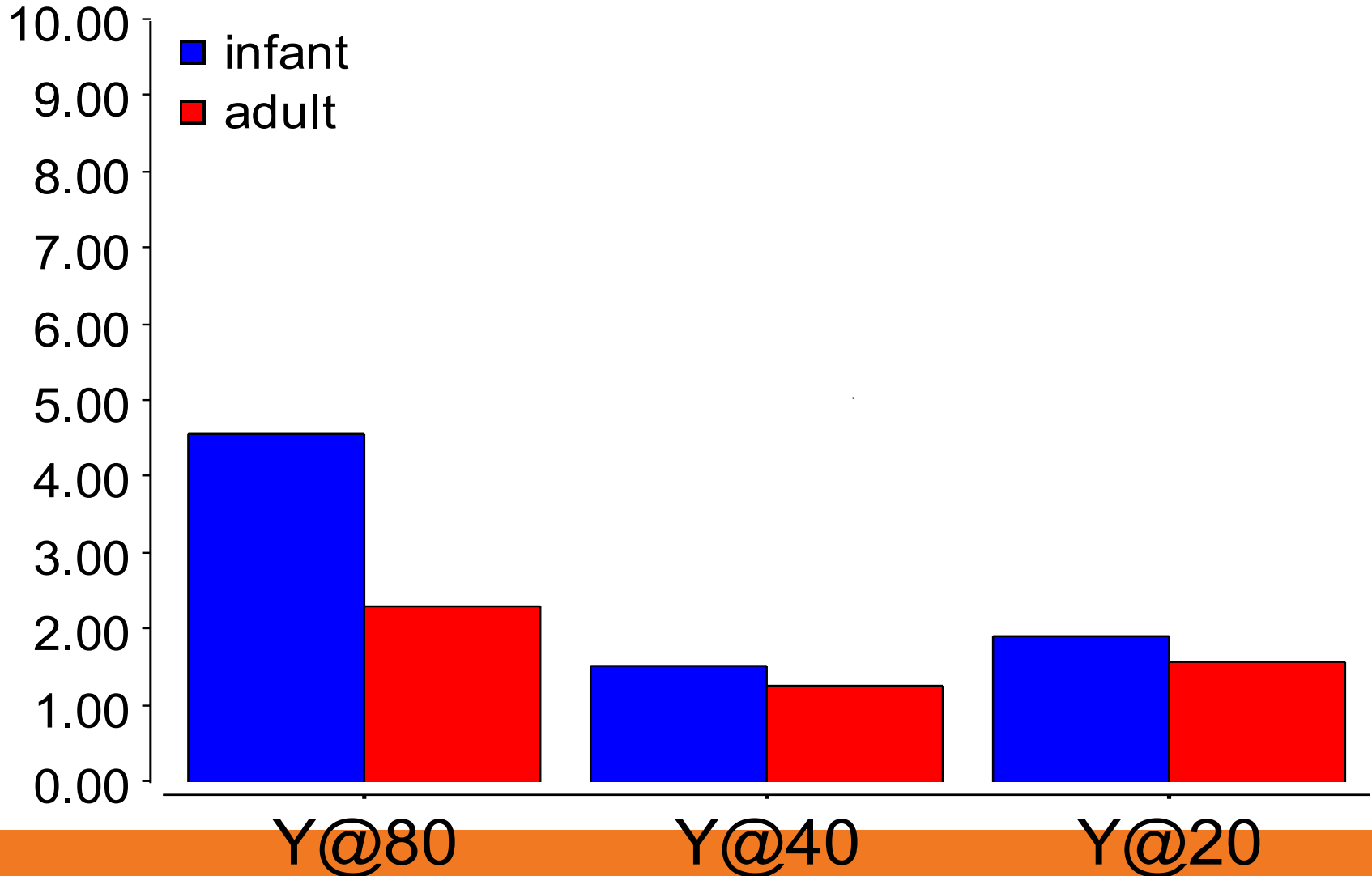
Adults vs Infants 20Hz



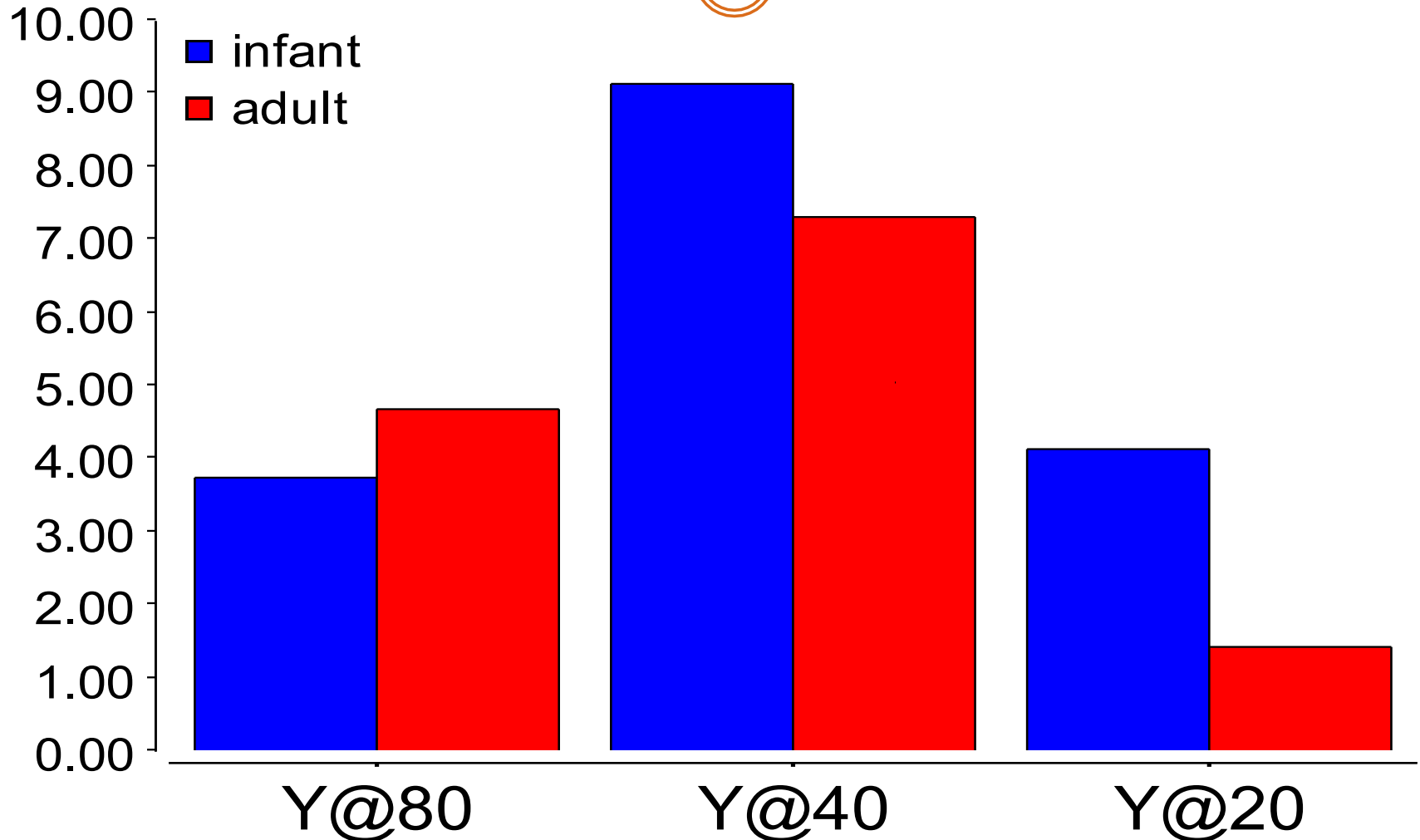
Amplitude, peak-to-peak



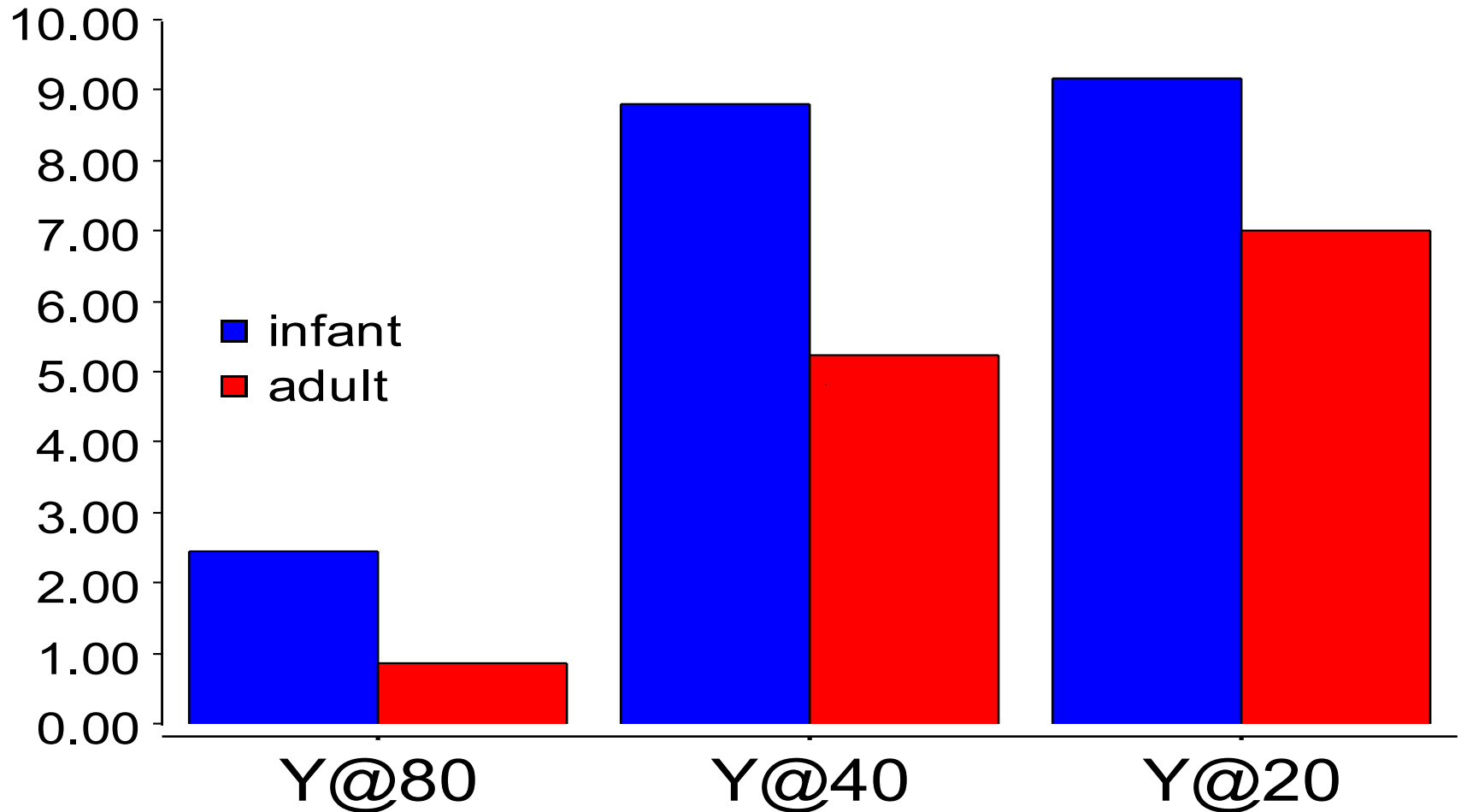
80 Hz Spectral Peak Levels



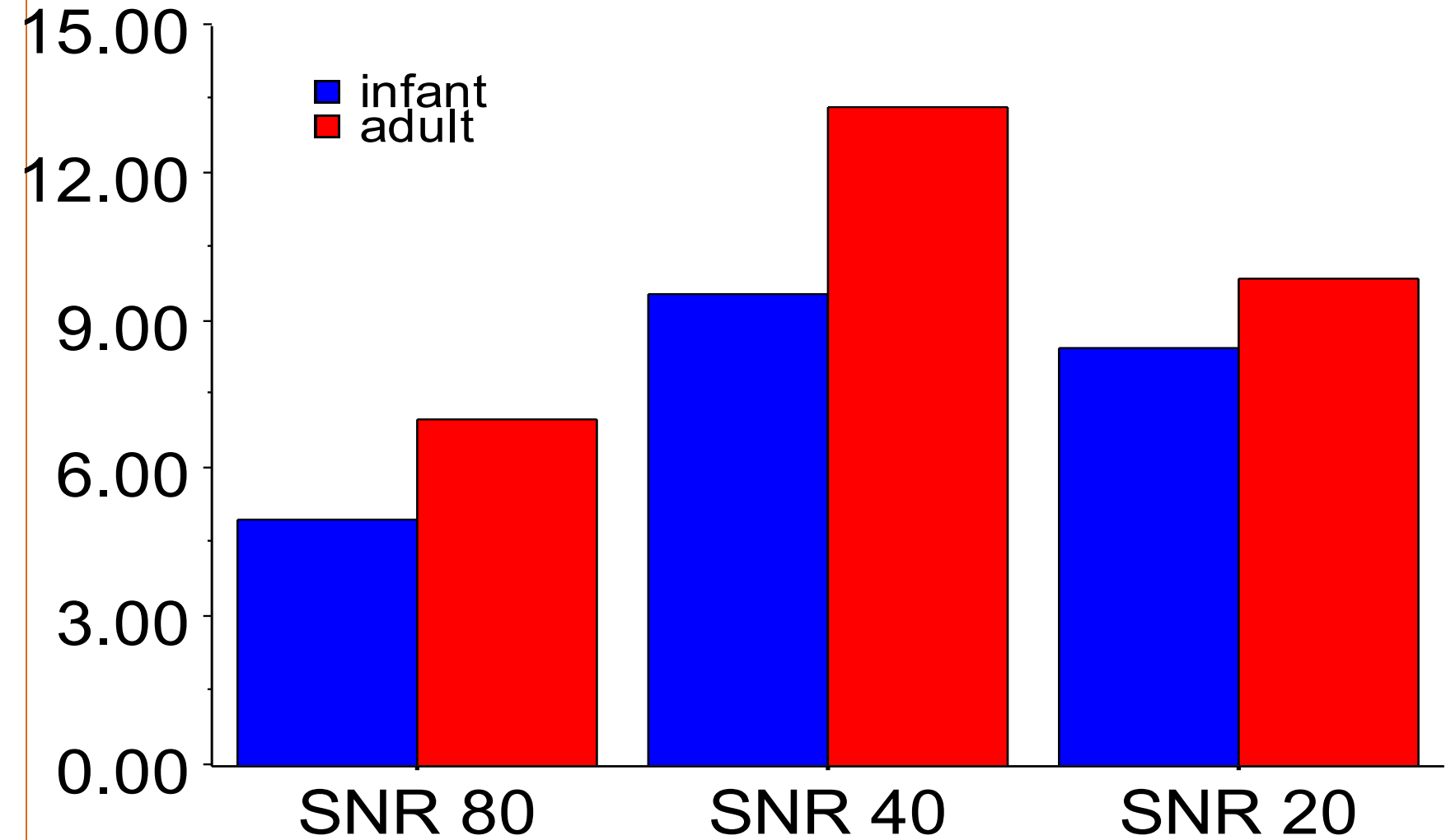
40 Hz Spectral Peak Levels



20 Hz Spectral Peak Levels



Spectral Peak SNR



Summary and Discussion



- ✓ Hypothesis 1
 - 80, 40 and 20 Hz responses were present at supra-threshold levels in infants tested while awake.
 - In awake infants, the SNRs for 20 and 40 Hz responses are larger than that for 80 Hz.
- ✓ Hypothesis 2:
 - Infants had larger peak-to-peak amplitude responses owing to higher residual noise, but poorer SNRs than adults. More harmonics observed for infants at 20 Hz.

Comparisons to other work



- Tlumak et al (2012) reported significantly lower spectral magnitude responses in 6-9 year old children compared to adults at 20 and 40 Hz.
 - Infant SNRs of >70% of adult values were obtained.
- Riquelme et al (2006) reported ASSRs present at mfs of 20-90 Hz in neonates, but with peak SNRs were at 70-90 Hz.
 - Infant SNRs were highest at 40 Hz and lowest at 80 Hz.

Slow Rate ASSRs



- Generator site is likely primary auditory cortex owing to dramatic differences observed by other investigators during sleep.
- Robustness of responses in awake infants matches that we have observed in the transient CAEP.
- ASSRs at 40 Hz may have some advantages over transient MLR or CAEP responses for estimating threshold and temporal processing abilities in young infants.