Types of Hearing Loss

- **Peripheral**
  - Conductive
  - Sensorineural
- **Central**
  - Auditory Processing Disorders
  - Tinnitus
  - Hyperacusis

How do we test hearing in mice? (overview)

**High through-put**

- Evoked potentials & Emissions: auditory brainstem response (ABR), distortion product otoacoustic emissions (DPOAE)
- Reflexive measures: Preyer reflex, acoustic startle response (ASR), prepulse inhibition (PPI)

**Low through-put**

- Trained behavioral tasks: positive reward conditioning, conditioned avoidance

Auditory Brainstem Response (ABR)

- Synchronous evoked response of a population of auditory neurons to the onset of a sound stimulus.
- Subcutaneous electrodes placed near the ear and vertex of the skull in anesthetized animal.
- Stimuli: brief tone pips/clicks
- Average response over many repetitions.
- NOTE: Electrode placement, anesthesia, body temperature can affect ABR.
Auditory Brainstem Response (ABR)

ABR Threshold Measurement: Example

Measure threshold (lowest sound level that elicits response) for tones of different frequencies and broadband clicks.

ABR audiogram: Example

Limitations of ABR test

- ABR test is NOT a perfect predictor of animal’s actual hearing ability.
- ABR thresholds are higher (10 - 30dB SPL) than behavioral thresholds in mammals (Gorga et al., 1988).
  - ABR uses a very brief stimuli (5-10 msec)
  - Temporal summation
  - Differences in conscious responsiveness
Distortion product otoacoustic emissions (DPOAEs)

- Miniature speakers and microphone inserted into ear canal.
- Two tones (F1 and F2) are played to ear, and DPOAE at 2F1-F2 frequency is measured.
- Outer hair cells generate distortion products that can be measured with microphone.
- Reduced or absent DPOAEs indicate outer hair cell damage.
- DPOAEs can be used in combination with ABRs to isolate the site of damage.
- NOTE: Middle ear status can affect DPOAE.

Reflexive Measures

Preyer Reflex
Acoustic Startle Response (ASR)
Prepulse Inhibition (PPI)

“Click box” Test: Preyer Reflex

Pinna or whole body startle response to Hand Clap or Click Box stimuli. Used to screen profound hearing loss.

Pros:
- Fast/easy screening
- No training required

Cons:
- Crude way of testing deafness
- Fails to identify mild/moderate hearing loss
- Experimenter Subjectivity (False Positive)
- Choice of Stimulus (False Negative)
- Dependent on motor function

Does Lack of Preyer Reflex always indicate Hearing Loss?

Mutant (-/-) mice show normal ABRs

Limitation of Preyer Reflex Test

Mutant (-/-) mice show normal ABRs

Preyer Reflex test is NOT a sensitive hearing test.

Cunningham et al., 2017

Cunningham et al., 2017

Cheatham et al., 2001

Kiernan et al., 1999

Kleinman et al., 1989
Acoustic Startle Response (ASR)

- Can test hearing function, noise-related anxiety, habituation, hyperacusis.
- Does not require learning/motivation.
- Easy to implement.
- Lack of startle does NOT necessarily indicate deafness or hearing impairment. (motor problem?)
- ASR can be affected by many factors: Strain, Hearing Status, Sex, Age, Stimulus parameter, Stress level, Handling, Non-auditory stimulus etc.
- Consistency is critical!

Pre-Pulse Inhibition (PPI)

- ASR can be modulated by pre-pulse stimulus.
**Modified PPI: Gap detection**

### Control Trial
- Startle Stimulus (< 20ms)
- (105dB)
- Background Noise

### Startle Stimulus
- Gap (1-10 msec)

→ Gap detection assess temporal processing.

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**Prepulse-Inhibition (PPI) and Modified PPI**

- PPI: tone pre-pulse reduces size of startle.
- Modified PPI: can test complex hearing functions (temporal processing, frequency/level discrimination).
- Does not require extensive training.
- Hearing status, age, sex, strain, behavioral state can affect result.
- NOT every task matches to perceptual performance.
- Optimization of the pre-pulse stimulus is important.
- Habitation/Sensitization/Potential Learning effect.

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**Gap Detection Example:** Temporal Processing Deficit

- Ison et al., 2017
- Oertel et al., 2017

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**Trained tasks: Positive reinforcement**

- Can test complex hearing functions, such as pitch perception, frequency discrimination, sound localization etc.
- Takes a long time to train the animal.
- Requires learning and motivation.
- Requires food or water deprivation.
- Not suitable for very young mice/or mice with hearing loss (aging).
- Other tasks: nose-poke, lever-press.
Trained tasks: Conditioned avoidance

- Water deprived mouse is trained to lick spout for liquid reward in the presence of target tone stimuli.
- If animal licks the spout during background noise a mild shock will be delivered.
- May not be appropriate for hyperactive or hypoactive mice.

Auditory Phenotyping: Considerations

Mouse vs. Human Audiogram

Hearing Development in Mouse

Variation in Hearing Across Strains

Age-related Hearing Loss in Different Strains

- CBA/CaJ maintain good hearing until 2 years of age.
- C57BL/6 and DBA/2J have age-related hearing loss with different progression pattern.
- Other strains also show age-related hearing loss (BALB/c, 129s, CD1)
Vivarium/Environmental Noise?

Most of the noise in the vivarium is generated by humans.
Quite/low-noise environment is recommended.

<table>
<thead>
<tr>
<th>Weekday Low Frequency (10 Hz – 12.5 kHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekday High Frequency (12.5 – 70 KHz)</td>
</tr>
<tr>
<td>Weekend High Frequency (12.5 – 70 KHz)</td>
</tr>
</tbody>
</table>

Summary

- Use appropriate hearing test(s) to identify auditory phenotype.
- Pay close attention to the strain, age, and other factors that can affect the results.
- Your mutant mice may have something to offer the hearing science community.

Thank You!

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