The Effect of Gene Mutations on Neural Response of the Electrically-Stimulated Auditory Nerve in Children

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Background

- Hereditary hearing loss due to genetic mutations (a.k.a. genetic deafness) accounts for approximately 50-60% of congenital hearing loss, affecting approximately 1 in 1000 newborns in the United States.

- The association between genotypes and auditory-neural-function phenotype has not been systematically investigated.
Study One: Aim

• To examine the neural response of the electrically-stimulated auditory nerve (i.e., the eCAP) in pediatric cochlear implant (CI) users with Gap Junction Beta-2 (\(GJB2\))- or Solute Carrier family 26 member 4 (\(SLC26A4\))-related hearing loss, and compared their results with those measured in children with idiopathic hearing loss.

• Mutations in \(GJB2\) and \(SLC26A4\) genes are the most commonly identified causes for genetic deafness, accounting for around 37% of these cases (Jiang et al., 2015).
Study One: Subjects and Electrodes

- 55 implanted children with Cochlear® Nucleus™ devices
  - 20 children with biallelic *GJB2* mutations (G1-G20)
  - 16 children with biallelic *SLC26A4* mutations (S1-S16)
  - 19 children with idiopathic hearing loss (C1-C19)

- Testing Electrodes: one basal, one middle and one apical electrodes
  - e3, e12 and e21
Study One: eCAP Measures and Data Analysis

• Stimulus: biphasic, charge balanced electrical pulse
  • Cathodic-leading
  • Anodic-leading

• Dependent variables include the eCAP threshold, the maximum eCAP amplitude and the slope of the eCAP Input/Output (I/O) function.
Study One: Results

- Lower eCAP thresholds were measured for the anodic-leading than the cathodic-leading biphasic pulses.
- Subjects with GJB2 or SLC26A4 gene mutations showed higher eCAP thresholds than subjects with idiopathic hearing loss.
Study One: Results

- Larger maximum eCAP amplitudes were measured for the anodic-leading than the cathodic-leading biphasic pulses.
- Subjects with \textit{GJB2} gene mutations showed larger maximum eCAP amplitudes than subjects with \textit{SLC26A4} gene mutations and subject with idiopathic hearing loss.
Study One: Results

- Steeper slopes of the eCAP I/O function were measured for the anodic-leading than the cathodic-leading biphasic pulses.
- Subjects with *GJB2* gene mutations showed steeper slopes of the eCAP I/O function than subjects with *SLC26A4* gene mutations and subject with idiopathic hearing loss.
Conclusions

• Anodic stimuli are more effective in activating the auditory nerve fibers than cathodic stimuli in spite of GJB2 or SLC26A4 gene mutations.

• Children with hearing loss caused by the GJB2 gene mutation have better neural function than those with the SLC26A4 mutations and concurrent Mondini malformation and EVA or idiopathic hearing loss.
Study Two:

• **Aim:** Study Two examines sensitivity of the electrically-stimulated auditory nerve to amplitude modulation in patients with myosin XVA (MYO15A) mutations.

• **Subjects:** Two girls with MYO15A mutation with Cochlear® Nucleus™ devices.

• **Testing electrodes:** e3, e12 and e21.

• **Amplitude modulation rates tested:** 20 and 200 Hz.
Study Two: Preliminary Results

Time (ms) - 200 AM pulse train

Time (ms) - 20 Hz AM pulse train

M1, e21

M2, e21

1 pulse
20 Hz
200 Hz

eCAP amplitude (μV)
Thank you!