Image-abnormal cochleovestibular nerves in pediatric patients with hearing loss: hearing, imaging and genetic data

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Study Design

• Retrospective review
• 37 children bilateral abnormal cochleovestibular nerves (CVNs), 3 unilateral
• 77 total ears with abnormal CVNs evaluated
• 22 males, 18 females
• 18 (45%) with comorbid conditions/disabilities
  • 1 CHARGE, 1 VACTERL, 1 Goldenhaar
• 69 ears with available hearing outcomes data
Imaging Review

- MRI +/- CT
- Cochlea
- Vestibule
- SCCs
- Cochlear aperture size
- IAC diameter
- # of nerves seen in cistern and in lateral IAC
Hearing Data and Genetic Evaluation

- Hearing data available on 69 ears with abnormal CVNs (aided and/or unaided with hearing aids, CIs, ABIs)
- Genetics evaluation performed on 10 families, 7 of which yielded novel information
Cochleovestibular Nerve Branching

- 2 nerves in cistern
- 4 in lateral IAC
- Where branching occurs is VARIABLE
- <4 = ????? function of nerves in lateral IAC

6 Casselman et al. 1997
Classification

- Aplasia, hypoplasia (Casselman)
- Deficiency (Buchman)
- Reclassification based on number of nerves in IAC?
  - Birman 2016
Birman, et al, 2016 Classification of Cochleovestibular Nerve Status

Normal
CVN abnormalities and Cochleovestibular Malformations

60 ears (82%) with absent or narrow cochlear aperture

37 ears (46%) NORMAL cochlear partitioning

Almost ALL had some CVM anomaly
Absent cochlea 12 ears (15%)
Vestibular anomalies 55 ears (69%)
Imaging Protocols - lack of concordance and consistency

- Gillard et al Poster Session
- Highly variable acquisition protocols
- Highly discordant interpretations on imaging results across centers
- Impact on surgeon decision making and insurance approval
Genetics of Abnormal Cochleovestibular Nerves

- Collaboration with USC, UCSD, TGen, Columbia, SUNY Downstate, Baylor
- 10 families (trios of affected child and parents) DNA/RNA collected from saliva whole exome sequenced
- Variants in several genes identified likely to affect otic capsule development: Six1, MASP1, GREB1L, HSPG2, TAF1, RIF1
- Two unrelated families with same de novo variant in Greb1L, animal model of Greb1L knockout exhibited absent CN8

Kari et al 2017, Schrauwen et al 2018
## Response to Sound Stimulation

<table>
<thead>
<tr>
<th>Test Device/ Response</th>
<th>Nerves in IAC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-Could not determine (n=19)</td>
</tr>
<tr>
<td>Unaided (19 ears)</td>
<td>0</td>
</tr>
<tr>
<td>Aided (51 ears)</td>
<td>3 (18%)</td>
</tr>
<tr>
<td>*Hearing Aid (29 ears)</td>
<td>CI 1/8 13% Birman 0 or 1</td>
</tr>
<tr>
<td>*Cochlear Implant (22 ears)</td>
<td></td>
</tr>
</tbody>
</table>
Response to CI/HA- Highly Variable

- 25/51 ears responded to sound stimulation (CI or HA)
- Average 59dB (25-95dB) in aided condition
- 3 subjects achieved closet set speech recognition between 6-24 mo after CI activation (all 3 with Birman 3 or 4)
- 1 achieved open set (Birman 3)
- Young age, language still evolving, not all patients received CIs
- Those that received ABIs had hearing outcomes similar to those that received CIs
Sound Awareness ≠ Language

• Language development is multifactorial
• FEW children in this cohort developed meaningful language
• Majority require sign and/or total communication
• How much benefit is sound awareness?
• How do we define benefit? Need to examine outcomes other than language, QOL?
<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (n)</th>
<th>Affected Ears (n)</th>
<th>Device</th>
<th>Nonusers n (%)</th>
<th>Unaided</th>
<th>Aided (HA)</th>
<th>Aided (CI)</th>
<th>Closed Set Speech Recognition</th>
<th>Open Set Speech Recognition</th>
<th>Average CAP/IT-MAIS (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birman 2016</td>
<td>50, (11 unilateral)</td>
<td>59</td>
<td>CI</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>NA</td>
<td>73% some spoken language</td>
<td>CAP Range 0-7 -Aplasia 47% -Hypoplasia 89%</td>
</tr>
<tr>
<td>Bradley 2008</td>
<td>6</td>
<td>6</td>
<td>CI</td>
<td>1 (17)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>37</td>
<td>83%</td>
<td>17%</td>
<td>CAP 2.3 (2-4)</td>
</tr>
<tr>
<td>Buchman2011</td>
<td>22</td>
<td>21</td>
<td>CI</td>
<td>4 (18)</td>
<td>99</td>
<td>71</td>
<td>49</td>
<td>NA</td>
<td>19%</td>
<td>NA</td>
</tr>
<tr>
<td>Chao et al., 2016</td>
<td>10</td>
<td>10</td>
<td>CI</td>
<td>Not reported</td>
<td>NR</td>
<td>81</td>
<td>44</td>
<td>NA</td>
<td>NA</td>
<td>CAP 70% 4+</td>
</tr>
<tr>
<td>Colletti, L 2013</td>
<td>21</td>
<td>21</td>
<td>CI to ABI</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>NA</td>
<td>NA</td>
<td>CAP 4.3 (2-7)</td>
</tr>
<tr>
<td>Govaerts 2003</td>
<td>4</td>
<td>4</td>
<td>CI</td>
<td>2 (50)</td>
<td>NR</td>
<td>Not reported</td>
<td>50% NR 50% 40-60</td>
<td>25%</td>
<td>25%</td>
<td>NA</td>
</tr>
<tr>
<td>Kang 2010</td>
<td>6</td>
<td>6</td>
<td>CI</td>
<td>1 (17)</td>
<td>50% NR 50% 99</td>
<td>Not reported</td>
<td>Not reported</td>
<td>17%</td>
<td>NA</td>
<td>CAP 3.9 (2-5)</td>
</tr>
<tr>
<td>Kutz 2011</td>
<td>9</td>
<td>10</td>
<td>CI</td>
<td>Not reported</td>
<td>17% NR 83% 55</td>
<td>Not reported</td>
<td>36</td>
<td>11%</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Morita et al., 2004</td>
<td>20</td>
<td>20</td>
<td>CI</td>
<td>Not reported</td>
<td>Profound</td>
<td>Not reported</td>
<td>Not reported</td>
<td>NA</td>
<td>NA</td>
<td>IT-MAIS 22.3 @ 1yr</td>
</tr>
<tr>
<td>Vincenti et al., 2014</td>
<td>5</td>
<td>5</td>
<td>CI</td>
<td>-0-</td>
<td>102</td>
<td>88.3</td>
<td>45.2</td>
<td>NA</td>
<td>20</td>
<td>NA</td>
</tr>
<tr>
<td>Wu et al., 2014</td>
<td>15</td>
<td>15</td>
<td>CI</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>NA</td>
<td>NA</td>
<td>CAP 4.3 (0-6)</td>
</tr>
<tr>
<td>Young 2012</td>
<td>10</td>
<td>10</td>
<td>CI</td>
<td>2 (20)</td>
<td>91</td>
<td>50% auditory sensation</td>
<td>10% NR 90% 32</td>
<td>10%</td>
<td>30%</td>
<td>NA</td>
</tr>
<tr>
<td>Zhang 2012</td>
<td>9</td>
<td>9</td>
<td>CI</td>
<td>Not reported</td>
<td>&gt;100</td>
<td>89% &gt;85 11% 74</td>
<td>56% NR 44% 60</td>
<td>NA</td>
<td>NA</td>
<td>CAP 2.3 (1-5)</td>
</tr>
</tbody>
</table>
Conclusions

- CVN abnormalities strongly associated with CVMs but CAN present with normal anatomy
- MRI is essential in diagnosis
- Birman classification shows trends towards predicting outcome but no imaging findings predict response to intervention
- Birman 0– guarded expectations
- Imaging Protocol Guidelines for Pediatric SNHL
- CI before ABI, some centers do concurrent
- Genetics are complex but long-term may aid in management