Consequences of UHL on Language and School Performance

Judith E. C. Lieu, MD MSPH
Phonak Unilateral Hearing Loss in Children Conference
October 23, 2017
“Historically, the involvement of hearing health professionals in the management of children with unilateral hearing loss has been limited. The conventional approach was to identify the cause of the hearing loss and to assure the parents that there would be no handicap.”

Oyler, Oyler & Matkin, 1987
Prevalence of UHL in Children

• Prevalence of UHL increases with age
• Newborns—about 1 in 1000\(^1\)
  • ~1/3 of children with congenital hearing loss
• Adolescents—about 1 in 5\(^2\)
  • 19.5% with hearing thresholds >15 dB
  • 2.5% with hearing thresholds >25 dB

\(^1\)Lieu, Seminars Hearing, 2010
\(^2\)Shargorodsky et al, JAMA 2010
Overview of Consequences

- Speech-language outcomes
- Educational outcomes
- Behavior
- Quality of life
- Possible explanations
Speech-Language Consequences
Infants & Toddlers

• Delay in 1st 2-word phrase by parent recall\(^1,^2\)
  • 23.5 months (18-48), n = 31
  • 18.5 mo (109 UHL) vs 15.4 mo (95 sibs), p=.008

• Delay in auditory behavior & preverbal vocalizations\(^3\)
  • 34 infants with UHL (median age 9.4 mo)
  • 331 infants with normal hearing (median age 9.0 mo)
  • Auditory behavior (IT-MAIS) delayed in 21% UHL vs 4% NH, OR 3.86
  • Preverbal vocalization (PRISE) delayed 41% UHL vs 3.6% NH, OR 8.64

\(^1\)Kiese-Himmel, 2002; \(^2\)Lieu et al, 2010
\(^3\)Kishon-Rabin et al, 2015
Speech-Language Consequences
Preschool children I

• Delayed language development at age 4-6 years compared to normal hearing peers\(^1\) (n=58)
• Lower communication, motor skills and adaptive behavior scores in 10 children with mild HL/UHL compared to 74 with normal hearing\(^2\)
  • Similar comprehension & expressive language scores compared to 19 children with mod-profound BHL

\(^1\)Borg et al, 2002; \(^2\)Vohr et al, 2012
Speech-Language Consequences
Preschool children II

• Communication development (2015)\(^1\)
  • Early identified children with mild BHL and UHL (median age ID = 4.2 mo)
  • 24 mild BHL and 31 UHL compared to 45 NH
  • Assessed at 12, 24, 36, and 48 months old
    • PEACH, ELF, CHILD, MacArthur-Bates, MLU, CDI
  • Only CHILD scores worse at age 3 & 4 years

\(^1\) Fitzpatrick et al, Am J Audiol 24:349–353
Speech-Language Consequences
School-aged children

- Few differences compared to controls on battery of 6 standardized language tests\(^1\) (n=25 cases)
- Language & auditory development\(^2\)
  - 21 children with profound UHL compared with 42 with NH (5-15 yo)
  - Lower scores on morphology, syntax, vocabulary in children with profound UHL
  - Similar performance on short term and working memory

\(^1\)Klee & Davis-Dansky, 1985
\(^2\)Sangen et al, 2017
Speech-Language Consequences
School-aged children

• UHL in Children, 6-12 year olds
  • 74 children with UHL vs. 74 sibling controls
  • Higher odds of speech-language therapy
    • 42% of children with UHL
    • OR 2.6, 95% CI 1.3-5.4
  • Lower scores on oral language skills
    • Language comprehension 91 vs 98, p=0.003
    • Oral expression 94 vs 101, p=0.007
    • Oral composite 90 vs 99, p<0.001

Lieu et al, Pediatrics 2010
# Multivariable Regression

## Oral Composite

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>T value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>13.7</td>
<td>7.7</td>
<td>1.8</td>
<td>0.08</td>
</tr>
<tr>
<td>UHL</td>
<td>-5.7</td>
<td>1.7</td>
<td>-3.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Full sum IQ</td>
<td>0.6</td>
<td>0.06</td>
<td>10.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.7</td>
<td>0.4</td>
<td>4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female sex</td>
<td>3.8</td>
<td>1.7</td>
<td>2.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Poverty level</td>
<td>-4.3</td>
<td>1.3</td>
<td>-3.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Adjusted $R^2 = 0.56$

Effect size $\sim 0.3 - 0.4$ SD
### Cognition Scores

<table>
<thead>
<tr>
<th>Standardized scores (SD)</th>
<th>Right UHL</th>
<th>Left UHL</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vocabulary*</td>
<td>48.7 (11.6)</td>
<td>46.8 (10.8)</td>
<td>51.6 (10.2)</td>
</tr>
<tr>
<td>Verbal IQ*</td>
<td>101.6 (16.9)</td>
<td>100.1 (15.6)</td>
<td>105.5 (14.6)</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>100.3 (15.5)</td>
<td>99.1 (13.0)</td>
<td>102.6 (14.5)</td>
</tr>
<tr>
<td>Full IQ*</td>
<td>101.2 (16.0)</td>
<td>99.6 (14.2)</td>
<td>104.5 (14.3)</td>
</tr>
</tbody>
</table>

*Effect size ~ 0.2-0.3 SD

*p < .05 for any UHL compared to controls*
## Multivariable Regression

### Cognition scores

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>t value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Full IQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>85.8</td>
<td>3.7</td>
<td>23.2</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>UHL</td>
<td>-4.1</td>
<td>1.9</td>
<td>-2.1</td>
<td>.038</td>
</tr>
<tr>
<td>Maternal education</td>
<td>5.9</td>
<td>1.1</td>
<td>5.5</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Verbal IQ</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>85.3</td>
<td>3.9</td>
<td>22.0</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>UHL</td>
<td>-4.5</td>
<td>2.0</td>
<td>-2.2</td>
<td>.028</td>
</tr>
<tr>
<td>Maternal education</td>
<td>6.3</td>
<td>1.1</td>
<td>5.6</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
Nested Longitudinal Study

- Longitudinal study over 3 years, n=46
- Outcomes
  - Cognition—WASI
  - Language—OWLS
  - Achievement—WIAT-II-A
  - Behavior—CBCL
  - Hearing—audiogram
  - School records—IEP, speech therapy

- Multilevel regression modeling to analyze longitudinal outcomes

Standardized tests
Mean = 100, SD = 15

Lieu et al, Otol Neurotol, 2013
## Multilevel Model: Effect of Time (Age)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Initial Status (SE)</th>
<th>Rate of Change (SE)</th>
<th>Pseudo R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=46</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full IQ</td>
<td>98 (2.7)***</td>
<td>1.8 (0.6)**</td>
<td>0.11</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>96 (2.9)***</td>
<td>2.5 (0.8)**</td>
<td>0.13</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>100 (2.7)***</td>
<td>0.3 (0.6)</td>
<td>0.004</td>
</tr>
<tr>
<td>Listening comp</td>
<td>91 (2.4)***</td>
<td>1.0 (0.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Oral expression</td>
<td>85 (2.8)***</td>
<td>2.9 (0.7)***</td>
<td>0.19</td>
</tr>
<tr>
<td>Oral composite</td>
<td>85 (2.7)***</td>
<td>2.5 (0.7)**</td>
<td>0.16</td>
</tr>
<tr>
<td>Reading</td>
<td>104 (2.4)***</td>
<td>-0.2 (0.5)</td>
<td>0</td>
</tr>
<tr>
<td>Math</td>
<td>94 (2.8)***</td>
<td>0.5 (0.7)</td>
<td>0.007</td>
</tr>
<tr>
<td>Writing</td>
<td>100 (3.4)***</td>
<td>1.4 (0.9)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*p<0.05, **p<0.01, ***p<0.001

Lieu et al, Laryngoscope 2012
Oral Composite Score Model
Interaction with Full IQ
Verbal IQ Model
Interaction with IEP

![Graph showing the interaction between Verbal IQ and Age for children with and without IEPs, including lower and upper confidence limits.](image)
Education & Behavior
Effects of UHL

• Educational and/or behavioral problems\(^1\)
  • 22-59% receiving additional help (1980s-1990s)
  • 24-35% grade failures vs. 3% normally
• Compared to siblings with normal hearing\(^2\)
  • 4.4-fold increased risk of Individualized Educational Plans/Programs

\(^1\)Lieu, Arch Otolaryngol Head Neck Surg 2004
\(^2\)Lieu et al, Pediatrics 2010
Behavioral Outcomes—Longitudinal

- >20% scored ≤ 3rd percentile for Competency scales
  - Activities, Social, School, and Total
- 24% had academic area of weakness or executive function problems per teachers
- ~50% continued to have Individualized Educational Plans throughout the 3 years

Lieu et al, Laryngoscope 2012
# UHL and Adolescents

<table>
<thead>
<tr>
<th>Outcome</th>
<th>UHL (n=20)</th>
<th>NH (n=13)</th>
<th>Diff</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full scale IQ</td>
<td>98 (15)</td>
<td>112 (15)</td>
<td>14</td>
<td>0.017</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>101 (16)</td>
<td>113 (12)</td>
<td>12</td>
<td>0.032</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>95 (15)</td>
<td>107 (16)</td>
<td>12</td>
<td>0.037</td>
</tr>
<tr>
<td>Core language score</td>
<td>98 (16)</td>
<td>114 (10)</td>
<td>16</td>
<td>0.001</td>
</tr>
<tr>
<td>Expressive language score</td>
<td>100 (16)</td>
<td>114 (10)</td>
<td>14</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Verbal/Full IQ effect size ~0.8-0.9 SD  
Language Effect size ~ 1 SD
# Multivariable Regression: Language Scores

<table>
<thead>
<tr>
<th>Variables</th>
<th>Parameter estimate</th>
<th>SE</th>
<th>t value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Core language</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>52.1</td>
<td>16</td>
<td>3.2</td>
<td>.003</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>0.45</td>
<td>0.14</td>
<td>3.2</td>
<td>.003</td>
</tr>
<tr>
<td>UHL</td>
<td>-10.4</td>
<td>4.5</td>
<td>-2.3</td>
<td>.03</td>
</tr>
<tr>
<td>Health insurance</td>
<td>7.6</td>
<td>5.3</td>
<td>1.4</td>
<td>.159</td>
</tr>
<tr>
<td><strong>Expressive language</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>55.6</td>
<td>16</td>
<td>3.4</td>
<td>.002</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>0.46</td>
<td>0.14</td>
<td>3.2</td>
<td>.003</td>
</tr>
<tr>
<td>UHL</td>
<td>-8.8</td>
<td>4.6</td>
<td>-1.9</td>
<td>.064</td>
</tr>
<tr>
<td>Health insurance</td>
<td>5.5</td>
<td>5.3</td>
<td>1.0</td>
<td>.304</td>
</tr>
</tbody>
</table>
Child to Adolescent–Language Scores

- **UHL (6-12 year olds):**
  - Receptive
  - Expressive
  - Composite

- **NH (6-12 year olds):**
  - Receptive
  - Expressive
  - Composite

- **UHL (13-17 year olds):**
  - Receptive
  - Expressive
  - Composite

- **NH (13-17 year olds):**
  - Receptive
  - Expressive
  - Composite

**Statistical Significance:**

- *****P<0.001**
- ****P<0.01
- **P<0.05**
Child to Adolescent–Cognitive Scores

0.8-0.9 SD

***P<0.001
**P<0.01
*P<0.05

Verbal
Performance
Full

IQ Mean Scores

UHL NH UHL NH
6-12 years old 13-17 years old
Other Studies of Cognition

- Meta-analysis of IQ scores (2016)
  - UHL (n=173) compared to NH (n=202)
  - 6-18 year olds
    - Full IQ -6.3 (95% CI -9.1, -3.5)
    - Performance IQ -3.8 (95% CI -7.3, -0.2)
    - Verbal IQ -4.0 (95% CI -7.5, -0.4)

Purcell, Shinn, Davis, Sie. Laryngoscope 126:746–754
Quality of Life

- Individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns
- Hearing Environments And Reflection on Quality of Life survey (HEAR-QL)
  - Self-reported
  - Two forms: Children and Adolescent
  - Compared children with normal hearing, UHL, and bilateral hearing loss
Quality of Life in Children, HEAR-QL

- Family & Friends
- Activities
- School
- Feelings
- Score

- Normal Hearing
- UHL
- Bilateral HL
Quality of Life in Adolescents

Rachakonda et al, *Laryngoscope, 2014*
Summary: Speech/Language Consequences

• UHL associated with delays in acquisition of preverbal behavior, speech and language in infants and preschool children
• Some school-aged children may have speech and/or language delays
• Improvement in language over time, but no “catch-up” to sibling controls
• Risk factors for delays
  • Poverty, low maternal education, male sex, low IQ, hearing severity
Summary: Educational Consequences

• ↑ Grade failures
• ↑ educational assistance (IEPs)
• ↑ Behavioral issues
• ↑ Academic weaknesses per teachers
• Risk factors for problems
  • ↓ IQ
  • Poverty, parental education
  • Severe to profound HL
MRI Studies of Brain Inter-connections

• How does UHL influence the neural development responsible for language, cognitive, and executive functioning?

• Compared children with severe-to-profound UHL vs. NH siblings
  • 7-17 years old, normal cognition
  • White matter integrity
  • Functional connectivity within grey matter

• Diffusion tensor imaging (DTI) and Resting-state fMRI (rs-fcMRI)
  • 3.0 Tesla scanner
  • single scanning session
Diffusion Tensor Imaging

- Evaluates white matter tracts
- Measures diffusion of water molecules in brain tissue
  - Anisotropy: Faster diffusion when parallel to white matter tracts vs. perpendicular
  - Fractional anisotropy (FA)
    - $0 = \text{equal diffusion in all directions}$
    - $1 = \text{diffusion in only one axis}$
  - Mean Diffusivity (MD)
    - Ease of water diffusion averaged over all directions
    - Measured $0$ to $1$
<table>
<thead>
<tr>
<th>AUDITORY ROIs</th>
<th>UHL</th>
<th>NH</th>
<th>p-value</th>
<th>Right UHL</th>
<th>Left UHL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD subcortical white matter of Heschl's gyrus, right</td>
<td>0.637</td>
<td>0.591</td>
<td>0.048*</td>
<td>0.643</td>
<td>0.632</td>
<td>0.130</td>
</tr>
<tr>
<td>FA lateral lemniscus, left</td>
<td>0.364</td>
<td>0.446</td>
<td>0.001†</td>
<td>0.381</td>
<td>0.351</td>
<td>0.005*</td>
</tr>
<tr>
<td>FA subcortical white matter of Heschl’s gyrus, left</td>
<td>0.338</td>
<td>0.397</td>
<td>0.013*</td>
<td>0.365</td>
<td>0.315</td>
<td>0.009*</td>
</tr>
<tr>
<td>FA lateral lemniscus, right</td>
<td>0.392</td>
<td>0.457</td>
<td>0.025*</td>
<td>0.397</td>
<td>0.351</td>
<td>0.079</td>
</tr>
<tr>
<td>NON-AUDITORY ROIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MD Putamen, left</td>
<td>0.708</td>
<td>0.696</td>
<td>0.034*</td>
<td>0.715</td>
<td>0.703</td>
<td>0.081</td>
</tr>
<tr>
<td>FA anterior limb of the internal capsule, left</td>
<td>0.575</td>
<td>0.607</td>
<td>0.030*</td>
<td>0.571</td>
<td>0.578</td>
<td>0.093</td>
</tr>
<tr>
<td>FA centrum semiovale, right</td>
<td>0.468</td>
<td>0.503</td>
<td>0.015*</td>
<td>0.456</td>
<td>0.477</td>
<td>0.030*</td>
</tr>
</tbody>
</table>

Additional columns list values for right unilateral hearing loss (Right UHL; n = 13) and left unilateral hearing loss (Left UHL; n = 16); adjacent p-value column refers to p-values of Kruskal-Wallis tests between right UHL, left UHL and normal hearing (NH). Only parameters with uncorrected p-values < 0.05 are listed.

* Trend at p < 0.05 level; † Significant at p < 0.004 for auditory ROIs and <0.003 for non-auditory ROIs.

Multiple Logistic Regression
DTI Parameters, UHL, and Outcomes

• Speech therapy
  • FA left middle cingulate gyrus (negative)
  • MD left middle cerebellar peduncle (positive)
  • FA left middle cerebellar peduncle (negative)
  • FA right middle cerebellar peduncle (negative)

• Individualized Educational Program (IEP)
  • MD left Heschl’s gyrus (positive)
  • MD left superior temporal gyrus (positive)
  • FA left Heschl’s gyrus (negative)
  • FA left superior temporal gyrus (negative)
  • MD left posterior limb internal capsule (positive)
  • MD right posterior limb internal capsule (positive)

UHL– all negative associations
Resting State fcMRI

- Human brain represents 2% body mass, but consumes 20% body’s energy at rest
  - Task related increase in brain metabolism is usually <5% \(^{12}\)

- Spontaneous neuronal activity
  - Is not random physical or physiologic noise
  - Low frequency BOLD signal

\(^{12}\) Fox and Raichle, 2007 Nat Rev Neurosci
**Blood Oxygen Level Dependent Signal**

- Deoxygenated blood is paramagnetic and can distort surrounding magnetic field
- BOLD signal is inversely related to deoxygenated blood

Diagram:
- Neural activity
  - Vasodilation with increased delivery of oxygenated blood
  - MR signal
Functional Connectivity

- Regions of the brain with the same BOLD time course thought to be activated together, thus, functionally linked\textsuperscript{12}
- Low frequency BOLD (<0.1Hz) represents resting state or spontaneous neuronal activity

Fox and Raichle 2007 Nat Rev Neurosci
Interregional correlation analysis

- Resting state BOLD signal extracted from each ROI
- This time course correlated to time courses in each voxel of the brain (correlation seed map)
- The correlation seed map underwent Fischer transformation
- Z scores $>3$ ($p<0.001$) with cluster size greater than $459\text{mm}^3$ (Monte Carlo simulation) used to determine statistical significance
- $T$-tests performed on $Z$-maps between controls and RUHL, LUHL and combined UHL
Regions of Interest

- **Auditory**
- **Cingulo-Opercular**
- **Default Mode**

- **Fronto-parietal**
- **Phonological**
- **Sensorimotor**

- **Visual Processing**
- **Language Comprehension**
- **from Conjunction Analysis**
Conclusions—fcMRI Studies

- Differences in multiple networks
  - Auditory regions—middle temporal gyrus
  - Executive function regions—inferior frontal gyrus
  - Sensorimotor regions—lips, tongue, speech

- Differences in several networks related to task-level control
  - rapid/adaptive control (fronto-parietal)
  - sustained/maintenance control (cingulo-opercular)

Tibbetts et al, 2011
Conclusions II—fcMRI Studies

• Some higher order cortical functions affected by UHL
  • Adaptive changes? There were findings to support functional changes that may show compensation for hearing loss, such as utilizing visual processes, as well as language and motor regions to increase mental rehearsal
  • Maladaptive changes? Decreased connectivity changes within executive control networks and aberrantly increased connectivity changes between anticorrelated networks
  • May explain some educational and behavioral problems in children with UHL

Jung et al, Laryngoscope (in press)
Summary: Children with UHL

• High rate of speech therapy (approaching 50%)
• Language delays in infancy through adolescence, differences may widen
• Differences in verbal IQ differences do not disappear, may widen with increasing age

• Do children with UHL have permanent decrease in language and cognition (disability) or do they have slower acquisition (delay)?
• Can interventions mitigate or eliminate the consequences in children with UHL?
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  - American Otological Society
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